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Editorial

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Diabetes Mellitus: Without a diminished internal secretion of the pancreas there can be no true diabetes. That much is conceded both by clinicians and physiologists. Just how this pancreatic insufficiency affects the organism is the subject of much dispute. Von Noorden and his followers insist that the loss of pancreatic function is followed by a hyperexcitation of the sugar-releasing mechanism of the liver and a consequent over-flooding of the blood with glucose. Minkowski and his school, while conceding that there may be an abnormal production of sugar, due to tissue hunger, maintain that the prime factor in the disturbed metabolism of the diabetic is the inability to oxidize sugar in the tissues because of the deficiency or absence of the internal secretion of the pancreas. In either case, the pancreatic internal secretion is at fault.

By experiments on fifty-five dogs, in 1889 von Mehring and Minkowski established the following facts: (1). Complete removal of the pancreas invariably produces diabetes which persists until death. (2). If one-fourth or one-fifth of the gland is not removed, diabetes does not follow but it does follow removal of the remainder. (3). If a portion of the pancreas containing Islands and still attached to its arterial supply is transplanted under the skin of the abdomen and the remainder of the gland is afterward removed, no glycosuria is produced, but the removal of the transplanted portion is promptly followed by diabetes. Various other ingenious experiments have confirmed the above and have shown conclusively that absence of the internal secretion of the pancreas is the immediate factor in diabetes. The islands of Langerhans which furnish this internal secretion are very small glands found in the pancreas, especially in the "tail" or small end. They are not connected with the digestion of food in the duodenum, but furnish their secretion directly to the blood.

This internal secretion is probably a co-ferment or activator to the sugar oxidizing ferment present in the cells of the tissues. Like other ferments, this enzyme exists in an inactive form until it comes in contact with its co-ferment or activator. The absence of this activator prevents the utilization or combustion of sugar, which accumulates in the blood and is expelled in the urine.

That the combustion of sugar is accelerated by the internal secretion of the pancreas has been demonstrated by Knowlton and Starling in very original experiments. Their deductions were as follows: (1). The heart muscle of the dog, fed with normal blood, consumes about 4 milligrams of glucose per gram of heart muscle per hour. (2). This power of consuming sugar is reduced to a minimum or disappears altogether in hearts taken from animals which have undergone complete excision of the pancreas. (3). The addition of a boiled extract of pancreas to the blood circulating through the heart of a diabetic animal, restores to the latter the power of utilizing the glucose of the circulating blood.

Diabetes is a disorder of nutrition, according to Osler, and therefore too much stress should not be laid upon the likeness between diabetes experimentally produced and that resulting from years of faulty metabolic function. Apart from the existence of any specific disease that would cause organic change in the pancreas, it is evident that there must have been functional failure in other organs concerned in the many phases of nutrition. Recent investigations by that brilliant young pathologist, Nathan Mutch, have demonstrated that there is invariably a pathological condition of the duodenum in patients dying from diabetes mellitus and that the duodenal lesion probably precedes the pancreatic one. He also states that ileal stasis is usually present in diabetes mellitus and, in proportion to its severity, affects the prognosis adversely. As the duodenum holds the master-key to the most important digestive glands, Mutch's observations throw new light on the etiology of this disease.

Indigestion and Constipation are part of the history of most cases of diabetes mellitus. Besides the insufficiency of the internal secretion it would seem that the power of the pancreas to furnish the requisite ferments has been impaired, as there is faulty proteolytic and lipolytic digestion. Our readers may recall a discussion on "Diabetes in the Tropics" in the British Medical Association Section on Tropical Diseases in which it was pointed out and virtually agreed to by all present that all cases of diabetes in the tropics were preceded by derangement of digestion. As one speaker put it: "Practice in India impresses strongly on one the part dyspepsia plays in the production of glycosuria." Another speaker remarked that "it was no exaggeration to say that the agriculturists who live upon farinaceous food and who can ill afford to take meat or fish daily are almost immune against diabetes." Poverty and insufficiency of food do not cause the disease, nor does the ingestion of a large amount of carbohydrates, for it is an acknowledged fact that the coolies get very little proteid or fatty food in their dietary. The lazy and indolent rich are the chief sufferers.

These facts are very suggestive, and warrant the conclusion that diabetes is not the result of the over-ingestion of starchy food, but rather a condition beginning and ending with carbohydrate starvation—relative at first and finally absolute.

Former Errors in Regard to Diet: A great revolution has occurred in recent years in the diet of the diabetic. The change is somewhat bewildering to those who have not followed the question closely. From the starch-free diet, to "the oat-meal cure" is hardly more revolutionary than the recommendation of a dietary that reduces the consumption of meat to a minimum. Starting with a systemic hypoalkalinity, the result of overeating, particularly of a ration in which animal albumin and fat predominate and which eventually culminates in an attack of diabetes, it is too much to expect that the "acid" condition is to yield to a diet of animal proteid. An excess of animal proteid in diabetes has always to be reckoned with and the best authorities regard the still too common practice of allowing patients with glycosuria an unlimited amount of meat as highly pernicious in all cases. Indeed, glycosuria may often be caused to disappear entirely by the limitation of or abstinence from animal proteid. It is now recognized that the limitation of proteid in the dietary is of as much importance as the limitation of carbohydrate. Cammidge points out that faulty metabolism of proteins and fats may be the cause of more serious symptoms than the defective utilization of the carbohydrates. He therefore recommends that greater attention should be paid to nitrogenous metabolism. Cammidge says that it is impossible for a case of diabetes to make substantial improvement until nitrogenous equilibrium has been established.

Eccles says: "The very men and women whose daily food comes most nearly up to the standard of diet prescribed for diabetics are the very men and women in whom the cases of diabetes are most numerous and most fatal. They are the people whose daily ration is filled with fish, flesh and fowl, and in which but little room is left for bread or potatoes. . . . With an increase in the wealth of a nation comes an increase in the number of cases of diabetes, and with this, a decrease in the consumption of carbohydrates." That is sound philosophy, besides being a strong indictment of the high proteid dietary in the treatment of diabetes. It lends additional force to the dictum uttered by the same author: "Diabetics, like normal human beings, can get along well only on a normal diet."

Organotherapy in Diabetes: That the use of an appropriate extract of the pancreas is of service in the treatment of diabetes has been conclusively shown by the Italian worker, Massaglia. Massaglia's experiments (*Gazzetta degli Ospedali e delle Cliniche,* August 10, 1915), show that feeding a pancreas extract to animals suffering from glycosuria after pancreatectomy arrested or decreased the amount of glucose in the urine. When the animals were fed with meals containing 30 grammes of glucose, the urine always contained sugar, whereas when 30 c. c. of the appropriate pancreas extract were added to the same meals, the urine of one of the dogs was almost always normal. In the urine of the other dog only traces of sugar were found.

Various French observers have testified to the efficacy of certain pancreas extracts in true pancreatic diabetes, and their work has received additional confirmation by the clinical observations of the writer of the first of the "Articles of Interest" appearing in this number of "THE METABOLIST." This form of organotherapy is being recognized more and more as a reliable agent, and it is not too much to say that as familiarity with it increases, it will be still more widely used.

Dr. Tom A. Williams of Washington, in International Clinics, (Vol. 2, Series 36) discusses "The Management of Some Confusional States." One of the cases cited by Williams was a post-influenzal condition with exhaustion. This patient, when referred to the author, was taking caffeine, strychnine, sparteine and adrenalin solution. Williams recommended that the stimulants should be dispensed with, but that the adrenalin should be continued. Alluding to the adrenalin, he thought its effect might be improved by being taken along with one tabloid of Hormotone. When these measures were carried out, improvement was rapid, so that in four weeks the patient was able to be about.

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Contemporary Comment

THE PANCREAS AND SUGAR IN THE BLOOD.

In recent discussions of the causes of diabetes, two theories have gained prominence. *The Journal* has referred to them as the overproduction and non-utilization theories, respectively, using these terms in relation to the sugar factor, which naturally forms the essential theme for consideration in this disease. Whether or not it is agreed that the disturbance in the carbohydrate metabolism appears to represent a loss of power of oxidizing glucose, there is one fundamental fact about which no difference of opinion can exist. In diabetes, the sugar content of the blood is higher than normal and is variable in amount and, when it is sufficiently high, the glucose escapes through the kidneys into the urine. Hyperglycemia precedes the glycosuria.

At the department of physiology and pharmacology of the Rockefeller Institute for Medical Research, Kleiner and Meltzer have made a series of experimental observations that throw a somewhat different light on the subject of diabetes. Apparently certain striking differences in behavior occur between normal animals and those rendered diabetic by excision of the pancreas, a procedure which is familiarly known to result in glycosuria. Under physiologic conditions, sugar is liberated into the circulation from the liver, where it is stored as glycogen. If this function is imitated in an indirect way by the infusion of sugar solution directly into the circulation, the carbohydrate speedily finds its way out of the blood in some manner or other. Even a very large surplus of glucose will disappear from the blood stream under these circumstances. When the amount is large, part of the sugar is excreted through the kidneys, and part finds its way into the tissues. Before long the glucose content of the blood reaches nearly the same level which it had before the injection. Even in the absence of the kidney function, in nephrectomized animals, for example, the glucose returns to the previous level in about the same length of time, affording a striking example of the ability and readiness of the circulation of a normal animal to rid itself of a large surplus of sugar.

Quite different is the outcome of the introduction of sugar into individuals from which the pancreas has been removed. In such cases the blood is strongly hyperglycemic even before the sugar infusions. Kleiner and Meltzer found here, in contrast with what has just been recited, that the glucose content of the blood is not reduced promptly after the introduction of sugar. Apparently the removal of the pancreas interfered with the power of the circulation to rid itself readily of a surplus of glucose. The possible ability of the liver to provide the circulation with a greater supply of glucose in the absence of the pancreas can certainly be no important factor in these results. The investigators believe these new experiments to show that, in the presence of the pancreas, the circulation rids itself easily of intravenously introduced glucose, but that it is unable to do so satisfactorily in the absence of the pancreas. On the basis of these facts, Kleiner and Meltzer ask whether it is not plausible to assume, further, that the pancreas exerts exactly the same influence when the glucose in the circulation is being supplied in some other manner than by a buret into a vein—by the liver, for instance—through its connections with the circulation. In other words, do not these experiments make the assumption plausible that pancreatic hyperglycemia is due to the fact that, in the absence of the pancreas, the circulation is unable to dispose properly of the dextrose which it receives in normal amounts from the liver?

This is not all. The actual participation of the pancreas in the normal regulatory function is further suggested by the fact that the ability of the circulatory apparatus of animals to get rid of a surplus of glucose injected intravenously—a function which is impaired in the absence of the pancreas—can be temporarily restored by an intravenous injection of a pancreatic emulsion. Furthermore, such a procedure is also capable of reducing the hyperglycemia due only to depancreatization to a normal level of the sugar content of the blood.

It is too early to speculate extensively on the nature of the factors here involved. These interesting observations add one more link to the chain of evidence regarding the conspicuous performance of the pancreas in the disposal of sugar in the organism. Again, it becomes obvious that such effects of the pancreas must be of a chemical rather than a nervous character.—Editorial, *Jour. A. M. A.*, Oct. 2, 1915.

Occasionally I meet with men who are still living professionally in their undergraduate days, reading the same old books and writing the same old prescriptions, both blind and deaf to the changed environment. Fortunately the more intelligent of the public easily recognize these fossils and appraise them at their true worth.—V. C. Vaughan, M.D.

VITAMINE THERAPEUTICS IN DISEASES OF NUTRITIONAL DEFICIENCY.

It has been understood for some time that food, besides the ordinary elemental constituents, proteids, carbohydrates, and fats, must contain other materials in order that there may be orderly metabolism and proper nutrition of the body. This other material has been named vitamine. Although its exact nature has not yet been determined, it has been amply demonstrated that unless it is present in the food in sufficient quantities, gross nutritional disturbances of an ultimately rapid fatal character may develop. . . .

All food products contain vitamines. Some are rich in them, others very poor. In others the vitamine is abstracted or destroyed in the various food preparation processes. In a mixed diet there is enough vitamine to keep up the nutrition. It does not matter, therefore, that large quantities of food are consumed; unless the food has sufficient vitamine principles there will be starvation. This is the case among the poor who, while they consume large quantities of food, do not have sufficient mixture to give them an adequate amount of vitamine. Hence the reason for so many malnutritional conditions among them. . . .

. . . Little progress had thus far been made in the isolation of the vitamine principle in sufficient quantities to be of value therapeutically because most of the vitamine was lost, destroyed, or rendered inert in the processes of isolation. But the recent experiments carried out in the Hygienic Laboratory (Bulletin, February 18, 1916) on the vitamine content of brewer's yeast gives hope of great results. Heretofore the great difficulty had been to isolate the vitamine in sufficiently concentrated amounts to make it practically of use as a medicament. This problem was solved by the use of Professor Lloyd's prepared hydrous aluminum silicate, which has a very high selective absorptive power. It was found that 0.05 gram of this solid vitamine product would keep in health a 300 gram pigeon fed exclusively on polished rice, or would cure in a very few hours pigeons that had already manifested polyneuritis on this diet. Control pigeons fed on polished rice and untreated with vitamine soon died with polyneuritis. . . .

. . . It is now to be hoped that the isolation of vitamines from other food products rich in them will soon be accomplished.—Editorial, *N. Y. Med. Jour.*, March 18, 1916.

THE TESTES AND THE SYMPATHETIC SYSTEM.

. . . We may properly speak of "genital hormones" in explanation of the undoubted chemical correlation exerted by the genital glands on other parts of the reproductive apparatus as well as on the organism in general. At any rate, the secondary sexual characters must be associated with the influence of chemical substances produced by the ovary and testis, respectively. Castration after puberty cannot modify profoundly the development of structures like the skeleton, which are already completed; but it may bring about obvious structural and even functional changes which can be determined by careful observation.

The fact that phenomena of the sort here discussed are actually under the dominance of hormones, rather than the effect of alterations in the nervous communications between the parts of the body concerned, is demonstrable by direct experiment. Frequently the reimplantation of the missing tissue will restore a lost function or induce a return of normal manifestations. This has been seen in the case of the period of "rut," in the female, which has been abolished by extirpation of the ovary and reinduced by implantation in the peritoneum of an ovary from another animal of the same species.

The more intimate nature of the physiologic alterations involved in castration has remained largely a mystery because few detailed observations have been made on the phenomena by the critical methods of modern science. Recent studies have furnished evidence that changes in functional as well as morphologic processes follow the removal of the primary reproductive glands in the male. The circulatory reactions to nicotin, which consist ordinarily in a rise of blood pressure even with very small doses of the drug, are lowered as a result of gonadectomy. Recalling that the specific action of nicotin falls not on the central nervous axis but on the peripheral ganglions of the autonomic nervous system, it seems clear that castration exerts an influence on the sympathetic nervous outfit. Its irritability is decreased, and this may partially account for the changes in disposition in castrated animals. To these facts may now be added the further observation of a more or less complete restoration of the usual response to nicotin in the same (castrated) animals after implants of testicular tissue. The presence of successful testicular grafts in any part of the body seems to result in renewed activity of the vasomotor mechanism. . . . —Editorial, *Jour. A. M. A.*, May 13, 1916.

Articles of Interest

OBSERVATIONS ON THE DIAGNOSIS AND TREATMENT OF DIABETES.*

BY MARTIN M. BROWN, M. D., F. A. C. S.,
NORTH ADAMS, MASS.

Concerning the diagnosis and treatment of this malady, I have nothing original to offer, but will present a few facts gleaned from various sources. All authorities are agreed that the condition of diabetes mellitus is increasing; that it is a disease largely, but not exclusively, of the well-to-do. The malady occurs at all ages and in both sexes. Heredity plays a large part, and is traceable in at least 20%. Observers are agreed that functional or organic disturbances of the pancreas are the main causative factors. Experimental observation upon dogs shows that complete extirpation of this organ is invariably followed by diabetes. The conclusion is drawn that the pancreas supplies an internal secretion essential to carbohydrate metabolism. Evidence has been accumulated which shows that other organs besides the pancreas exert an influence upon this process. Disturbances of the thyroid gland, parathyroid, and suprarenal capsules are many times associated with glycosuria.

Normal sugar is present in the blood from 0.05% to 0.12%. In diabetes the amount varies from 0.16 to 1.16%. The kidneys are able to hold back sugar when it is present in normal quantity, but when the sugar concentration is increased, the kidneys are no longer able to hold the sugar back. Why does sugar accumulate in the blood? Two theories suggest themselves; one, that the diabetic cannot oxidize sugar; the other, that too much sugar is made. Normally, sugar is derived from carbohydrates, which make a very large amount of our food. That sugar may be formed from proteins has been demonstrated by many experiments.

Transient glycosuria, besides being caused by diabetic tendency, may be due to injuries, to febrile infectious diseases, to certain poisons, and to the excessive intake of sugar. In my own personal observation, I have met with several cases of transient glycosuria, due, undoubtedly, to the excessive use of sugar. In these instances, a proper regulation of diet in a short time rendered the patient sugar-free.

**Boston Med. and Surg. Jour.*, March 2, 1916.

The symptoms associated with diabetes are familiar to you all. The diagnosis is established when repeated examinations of urine show the presence of sugar. Generally speaking, we become suspicious that a person may be suffering from glycosuria when he complains of excessive and frequent urination, unnatural thirst, pruritus, vague affections of the nervous system, and digestive disturbances which are not otherwise explained. The presence of boils and furuncles are always suggestive of diabetic conditions. It is a well-established fact that all patients suffering from this disease have a marked lessened resistance, and the presence of sugar in the blood renders them especially prone to all kinds of infections.

The ideal treatment for any disease is the removal of the cause. In diabetes this is not possible for the cause is unknown. The condition should not be treated in a routine manner; cases differ and must be treated individually. In no disease is the patient to be warned more against quackery and quack remedies, for the harm of improper treatment cannot be well retrieved. Diabetes is a disease against which the plan of battle cannot be laid for a month or a year, but for a decade, or possibly a life-time.

Having determined that the patient has diabetes, after several urinary examinations, the next question to be considered is whether the case is mild, moderately mild, or severe. In mild cases, glycosuria disappears from the urine as soon as carbohydrates are eliminated from the diet. It is moderately severe when the sugar disappears upon restriction of the diet, but reappears when carbohydrates in minimum quantities are added. It is severe when sugar cannot be removed from the urine by eliminating all carbohydrates from the diet and restricting the intake of protein food. The essential point of the dietetic treatment consists in bearing in mind the impaired tolerance of the diabetic for carbohydrates by not overtaxing this tolerance. The power of assimilation for carbohydrates is not only conserved in the majority of cases, but increased.

Defective non-combustion or oxidation of carbohydrates, as well as of proteids, in diabetics brings about a condition known as acidosis, due to the presence of beta-oxybutyric acid, which accumulates in the blood, and together with its derivatives, acetone and diacetic acid, is eliminated in the urine. Acetone is also eliminated in the breath. When this condition is present, the patient is liable to develop diabetic coma. This coma is usually preceded by premonitory symptoms, such as restlessness, irritability, dizziness, pain in the limbs, headache and drowsiness.

The treatment of acidosis will depend largely on the previous history of the case. If the patient has been under competent observation, and has developed ketonuria on a strict diet, largely of proteids, he needs carbohydrates. Sodium carbonate should be given in large doses, frequently repeated until careful urinary tests show freedom from this condition. The treatment of diabetic coma must be prompt, energetic and intelligent. Free bleeding is oftentimes advisable, free elimination from the bowels with bitter salines, and the introduction into the blood, by every way possible, of alkalies.

The tendency of all diabetics to become infected with various maladies calls frequently for surgical intervention. No diabetic is considered a good surgical risk. In every case requiring surgical intervention, preliminary treatment, if possible, should be instigated. The urine should be made sugar-free, and the condition of acidosis eliminated; strictest aseptic precautions should be used. It is well to administer alkalies before an operation, whether diacetic acid is or is not present in the urine. The fear of operation upon diabetics has, in a great measure, subsided, and no up-to-date surgeon hesitates to resort to surgical methods of treatment in any diabetic case, when indicated.

My experience in the use of drugs or special remedies, with the exception of one preparation, is unsatisfactory. The continued and intelligent use of trypsogen in certain selected cases of a pancreatic type seems to have a beneficial influence.

CASE REPORTS.

Case 1. Mrs. J. C., married, age 62 years. Under observation past 10 years. Passing large quantities of sugar in urine when first came under my observation. Diet restricted. Trypsogen administered. Gradual improvement. At no time has sugar been absent from urine, but greatly lessened. Has not taken tablets for about 5 years, but keeps in fairly good health by restricted diet.

Case 2. Mrs. S. W., married, aged 60 years. Under observation past five years. Passing continuously large quantities of sugar in urine. Restricted diet; use of trypsogen. Still using tablets, and finds that condition becomes much worse if omitted.

Case 3. Mr. C., widower, about 50 years of age. Under observation three years. Sugar continuously present in large quantities.

Unable to restrict diet to any degree. Takes trypsogen tablets faithfully. Urine sugar-free at end of two years. Discontinued tablets, sugar returned. Sugar-free when resumed tablets. General health first class, but gradual loss in weight.

Case 4. Master L. S., 10 years of age. Under observation one year. Acute manifestation, no apparent cause. Attempted to restrict diet and placed on trypsogen tablets. No improvement. Referred to Dr. Joslin of Boston. Placed in Deaconess Hospital and Allen treatment administered. Became sugar-free in about one week. Allowed to return home in six weeks. Remained sugar-free when instructions were carefully followed. Sugar present at repeated examinations during past three months, at times. Sugar present in small quantities at present time in spite of starvation treatment one day a week, and restricted 5% diet. Outlook unsatisfactory.

Case 5. Mrs. R., age 58 years. Sugar present continuously in large quantities. Treatment—restricted diet, use of trypsogen tablets. Material improvement, but at no time sugar-free. General health at present time much improved over that of two years ago.

THE DUODENUM IN DIABETES MELLITUS*

By N. Mutch, M. D., M. A., M. R. C. P.

"It is usually considered that, in diabetes mellitus, the changes in the function of the pancreas form the basis of the greater part of the symptom complex. The inception of the morbid process, however, lies behind this pancreatic landmark, and evidence is brought forward in this present paper to show that specific lesions are present in the duodenum, which probably precede the dissolution of the pancreas.

"The vertical length of the duodenal shadow measured orthodiagraphically after a bismuth meal, is less than 3½ inches in healthy adults, being approximately equal to the length of two lumbar vertebræ with their intervening disks . . . in nine consecutive patients with severe diabetes mellitus, the mean vertical length of the duodenum was 3-1/9 vertebræ, the extreme being 3 and 3½. Considering adults only, the average length was 4 4/5 inches, and the extremes 4½ and

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The Practitioner, May, 1915.

5½ inches respectively. These figures represent a very great enlargement of the organ. Not only is this part of the alimentary canal elongated, but it is increased in calibre also, and on examination after death the walls can be seen to share the same change, being thick and fleshy, and of a somewhat milky appearance. The same alterations in structure can be traced in the upper portions of the jejunum. This enlargement is almost invariably associated with the ileal or colonic stasis, and in some patients delay is so extreme and the consequent modification of the lower bowel so advanced, that there can be no doubt but that alimentary stasis preceded the onset of diabetes. . . . The duodenal dilatation of such patients might reasonably be ascribed to the factors which produce this abnormality in simple intestinal stasis. In the majority of cases, however, the increase in size of the upper part of the small intestine is the predominant change in the alimentary canal, while lower bowel delay and duodenal regurgitation, although present, are not sufficiently pronounced to account for the enlargement. Fecal accumulation is evidently a common concomitant of diabetes mellitus, but not the sole determining factor although it may be a predisposing cause. . . . The intensity of the disease is here seen to be directly proportional to the degree of ileal stasis, although there are isolated exceptions to this rule in young people, in whom the presence of stasis is more difficult to determine. Almost all diabetic patients excrete indoxyl, indolacetic acid, and parahydroxyphenylacetic acid in their urine, in varying proportions. In constipated subjects, these substances arise either directly or indirectly from the actions of B. coli on tryptophan and tyrosin in the small intestines, and the amounts excreted serve as an index of the extent to which the ileum is infected with coliform organisms. In diabetes mellitus the excretion of these bodies does not bear an obvious relationship to the severity of the disease, from which fact it may be inferred that the gravity of the prognosis in diabetes with marked ileal delay, depends upon some condition other than the coincident infection of the small intestine with coliform organisms. It has been demonstrated by Sir Arbuthnot Lane, and confirmed by other observers, that stasis in the ileum impedes the passage of the chyme through the duodenum by producing obstruction at the entrance to the jejunum. . . . Such stagnation would be detrimental to a duodenum already injured by disease, and affords a reasonable explanation of the adverse effect of ileal stasis in diabetes."

Recapitulating the facts substantiated in his paper, Mutch says: "(1). Diabetes mellitus is associated with great enlargement of the duodenum, which cannot be accounted for wholly by coincident intestinal stasis. (2). A profuse growth of streptococcus brevis was obtained from the duodenum of a boy with severe diabetes mellitus. Such an infection has not been found in any other condition. (3). Ileal stasis is usually present in diabetes mellitus and, in proportion to its severity, affects the prognosis adversely. (4). The urine of patients suffering from diabetes mellitus usually contains one or more products of the action of Bacillus Coli on tryptophan and tyrosin.

"The suggested explanation of these phenomena is that chronic duodenitis is the determining factor in the production of diabetes mellitus, and that ileal delay increases the severity of the disease by causing stagnation in the duodenum."

Joughin had under his clinical observation at the Neurological Institute of New York, a girl of about 16 years who had been in excellent health until January, 1913, when she began to suffer from severe epileptic seizures with temporal headaches accompanied by vertigo and vomiting. Menstrual history: Commenced in February, 1913, at the age of 15 years and 8 months. The flow was moderate in amount and occurred regularly in February, March, April and May; then she had amenorrhea for four months after which the menstruation appeared irregularly. The body weight increased from 105 to 150 pounds. She was somnolent, complained of loss of hair, and showed marked muscular asthenia. In February, 1913, she had an attack of epilepsy—petit mal. The epileptic seizures occurred with increasing frequency and soon became nocturnal and developed into grand mal. During the days corresponding to the menstrual period she had vicarious hemorrhages from the mouth and nose. Examination of the nervous system was negative with normal reflexes. The eye grounds were normal and the visual field normal. The mammary glands were not at all developed. The hair of the head was very fine, no hair in the axilla. The skin was dry and scaly. The hands were thick with blunt fingers. She was inclined to obesity. No alimentary glycosuria. A diagnosis of hypopituitarism was made, which diagnosis was borne out by treatment with hypophyseal extract. After a short period the headaches began to disappear, the hair grew profusely, and the patient lost 26 pounds. During the eight months that have elapsed since treatment was instituted, she has not had a single epileptic seizure, although formerly they occurred several times a month.

Brief Abstracts

A Case of Pancreatic Insufficiency.—(*Quarterly Journal of Medicine,* October, 1915). This interesting case was under the observation of Spriggs and Leigh for 21 weeks in interrupted periods. The intake of food for 64 days was carefully noted and the urine and feces analyzed and compared with it. The amount of fat passed out in the bowel movements on admission averaged 302 grammes per diem for 4 days. This is the highest figure recorded for a case of uncomplicated pancreatic disease. The loss of energy in the form of fat in the movements formed a large proportion (25-59%) of the total caloric energy of the food, from 55 to 99% of the fat in the food being lost in the feces. The emulsified fat of milk was much better absorbed than the fat of butter, meat or cod liver oil and the percentage of fat absorbed was less when a large quantity of fat was given.

In experimental periods various ferments were used. These included fresh pig's pancreas, trypsogen, glycerine extract of pancreas, holadin, liquor pancreatis, papain and pankreon, which were given for periods of two or three days. *All except fresh pancreas and trypsogen irritated the intestinal tract and caused the patient serious discomfort.* With fresh pancreas the absorption of fat was decreased while it was being taken. With all of these ferments except trypsogen the bulk of feces was increased especially with the glycerine extract of pancreas, holadin and papain, and the fat absorption was not improved. When the fat in the feces was compared with that in the diet, even allowing for a wide margin of error, it appeared that with holadin, liquor pancreatis, papain and pankreon, less fat was absorbed than in the control periods.

Four tablets of trypsogen were given three times a day during the experimental period, the preparation having been given for the three preceding days in increasing amounts. An increased absorption of fat resulted, one-third more than when no trypsogen was included in the diet. The bulk of the feces was also reduced by 10%. The amount and nature of fat in the diet were practically the same in two periods.

* * *

Detoxication and a Vegetarian Diet.—In an address read before the Vegetarian Society of France, Guelpa said that in a vegetable diet as a means to detoxication of the organism we will find in a great measure the solution of one of the most interesting problems of hygiene and therapeusis. In all animal life the organism consumes and transforms food into energy and by this constant exchange the equilibrium of the organic functions is maintained, resulting in a harmonious physiological existence.

Overexertion of certain organs entailed by indulgence in food without considering whether a need for it exists and whether the organism is capable of eliminating it, is followed by a disturbance in the functional equilibrium. While it is true that the tissues are endowed with an elasticity which tends to nullify the result of indiscretions, that limit of elasticity is soon exceeded by constant indulgence. One of the greatest problems in hygienic living consists in maintaining as long as possible the elasticities of the tissues and the synergetic function of the various organs. Certain foodstuffs tax the organs to the utmost and they are particularly those which most tempt the high liver.

Goff has stated that diabetes has increased fourfold in frequency and in gravity during the past 30 years and he attributes this increase in morbidity to the excessive ingestion of sugar. While Guelpa cannot agree with him exactly as to this pathogenetic coefficient, it is beyond question that the increase—which also applies to the arthritic affections, such as gout, asthma, eczema—is the consequence of the perverted mode of living advocated by the pernicious theories which dominated the last century, the reactionary theories of the schools of Rason and Broussais. According to the old school the exhaustion and anemia characteristic of these diseases were to be met by suralimentation, thus adding to the fuel instead of diminishing it. In an address before the Congress in Brussels, Guelpa advanced the theory that hunger is not a manifestation of the organism's need for aliment with which to repair the damage done to the tissues, but is instead an expression of suffering due to an intoxication arising in the digestive tract. Similarly, thirst is not a manifestation of the need for fluids to equalize the humors of the body, but is an expression of the need for detoxication, as fluids are taken in to wash away the toxic products.

Present-day ideas of anemia are sadly in need of readjustment. We have been accustomed to regard anemia as a state of impoverished blood resulting from malnutrition, whether due to insufficient quantity or quality of food, or due to some disturbance of assimilation, and we have tried to combat this condition by suralimentation and, when possible, with life in the open air. Nevertheless grave cases of anemia are not benefited by this mode of treatment. Even fresh air is powerless to overcome chlorosis and it is interesting to note that chlorosis is most common among young girls in the country. When anemia is not due to a sustained loss of large quantities of blood or to some incurable organic lesion as cancer or tuberculosis, it is due to an intoxication which affects especially the red blood corpuscles. The danger of that intoxication is proportionate in the organism's ability to form new red blood corpuscles.

The first aim in the treatment should therefore be detoxication and we would soon be rewarded by seeing the prostration and the pallor disappearing. To obtain this result, instead of further clogging the tissues with poisons let us further aid the organism in defending itself. The alimentary intoxication accounts for four-fifths of the total intoxication. If we bear that in mind it may not seem so paradoxical to withhold from time to time nourishment from the anemic. The improvement will be noted first of all in an increase in the number of red cells and in an increase in the amount of hemoglobin. Martinet and Le Gendre give the following contraindications to meat diet: (1), acute or chronic enteritis, because it favors intestinal putrefaction; (2), gout, lithiasis, rheumatism, etc., because it leads to uric acid and other pernicious nitrogen compounds; (3), in arteriosclerosis, aneurism and atheroma, because it increases arterial tension; (4), nephritis, cirrhosis and hepatitis, as it causes congestion of the liver and increases the urinary solids; (5), in nervous diseases, since, in a measure, it stimulates the nervous system.

* * *

The Dietetic Treatment of Diabetes.—(*Lancet*, March 23, 1912). Cammidge says that the aim of modern treatment of diabetes is to balance the diet in such a way that nutrition is as perfect as possible without an unnecessary strain being put on the organs of metabolism in any direction. While the administration of carbohydrates in larger amounts than the defective metabolic powers of the diabetic can deal with is injurious, their permanent exclusion from the diet is often not only unnecessary but positively harmful. Some diabetic patients have a marked susceptibility to proteins, so that their glycosuria is diminished more by restricting the protein intake and allowing carbohydrates, than by excluding the latter altogether. As a rule, proteins of vegetables are found to be less harmful than those of meat, and periods of vegetable feeding may be advantageously introduced. Vegetable proteins, such as legumes, may replace meat to some extent in the ordinary diabetic diet. It is usually unwise to attempt to remove all starchy foods from the diet to render the urine sugar-free. Most patients will be found to do better when one variety is given alone than when several are taken together, and some kinds will generally prove to be more suitable than others. The next step is to reduce the nitrogenous food, until only 100, 80 or even 60 grm. of protein are being taken in the day and not more than 12 or 15 grm. of nitrogen are appearing in the urine.

No routine line of treatment, however sound it may be in principle, can be applied to all cases. The metabolic powers of each patient must be experimentally determined and the diet adapted to his peculiarities and requirements must be worked out—that is to say we must treat the patient, not the disease.

* * *

Protein Regulation in Diabetes Mellitus.—(*Medical Record,* May 20, 1916). Cornwall emphasizes anew the necessity of regulating definitely the protein ration both as to quantity and quality in the treatment of diabetes mellitus. He particularly emphasizes the regulation of the quality of the protein and says that this has for its object the protection of the body from injurious split proteins. It is accomplished mainly by excluding or restricting the articles which contain free purins and undesirable split proteins, and those whose protein is especially susceptible to the action of the saprophytic or putrefactive bacteria in the alimentary canal. This means excluding from the dietary or limiting in quantity the protein articles of animal origin, with the exception of milk and its products, and certain of the vegetables which contain purins in notable quantities.

* * *

Pathogeny of Diabetes.—(G. Delgado Palacios, *Medical Record,* March 25, 1916). All food which is not properly digested and absorbed is lost for the organism and gained for putrefaction. Overeating and rapid mastication overcharge the alimentary canal beyond its digestive capacity. The putrefaction increases and the noxious products of bacterial catabolism invade the organism and cause degeneration of the minute structure of the pancreatic gland. This process, a kind of vicious circle, goes on unnoticed until low carbohydrate tolerance appears, and later, diabetes. Experimental diabetes may be produced in a dog by means of fecal putrefaction and resorption, and the primitive phenomenon of the pathogenic mechanism of clinical diabetes is an excess of ammoniacal and acid putrefaction of the contents of the large intestine, and therefore, in accordance with this conception, diabetes must be considered as a disturbance of fecal origin. The disease being entirely external and bacterial is curable by external and bacterial methods, namely, prolonged fasting and restricted diet. Palacios says that the radical treatment is fecal disinfection by such agents as chemical antiseptics, dietetic and hygienic measures and by biological antagonism. The institution of a sanitary condition of the intestinal tract is the main treatment of the disease.

* * *

Morphological and Chemical Properties of a Fat Content in the Suprarenals in Delirium Tremens.—(*Journ. A. M. A.*, Vol. 63, No. 25). Hirsch found that the suprarenals of patients who died of delirium tremens contain less cholesterin than the suprarenals in other cases of sudden death. This leads the author to think that in delirium tremens the entire organism is overwhelmed by a toxic substance of as yet unknown composition, and it is probably this substance and not the alcohol which causes the delirium. These changes are not found in the suprarenals in chronic alcoholism, and he thinks, therefore, that it must be some substance plus the alcoholic poison to which the system succumbs in delirium tremens.

* * *

The Effect of Adrenalin on Healing of Wounds.—(*Med. klinik*, Dec. 5, 1915, p. 1359). Wildt states that the official 1-1000 solution of adrenalin was diluted 100 times, so as to get a concentration of 1 in 100,000. The wound is irrigated with this and packed with gauze dipped in the solution. The healing is hastened in a remarkable degree, the wound filling in fast with granulation tissue until it reaches the surface.

* * *

Transplantation of Testicles.—(*N. Y. Med. Journ.*, Nov. 14, 1914). Lydston reports the interesting observation on himself of transplantation of the testicles. He had had edema of one leg and eczema on the plantar surface which had defied all treatment. The edema disappeared and the eczema cleared up after the implantation of the gland. Lydston states that he has observed a case of psoriasis in which complete cure followed transplantation of the genital gland and he draws the conclusion that many cutaneous diseases are due to a perversion of the internal secretion of the generative organs.

TRYPSOGEN

The Logical Treatment of Diabetes Mellitus

Despite the complex conditions entering into the consideration and treatment of diabetes mellitus it is now conceded by all that faulty function of the internal secretion mechanism of the pancreas is the outstanding feature in the disease. But before functional or organic change takes place in the pancreas there must have been profound derangement of metabolism—usually the result of years of wrong living. The evidence shows that there is functional interference with the mechanism of digestion, absorption and elimination, and that intestinal stasis with a consequent severe intoxication is the prime factor which produces the derangement of the pancreas and other glands of internal secretion that are immediately concerned in the metabolism of starches, fats and proteins. In diabetes mellitus, as in kindred disorders, a decrease in the alkalinity of the blood and tissues has been observed by many investigators. This is usually the result of a faulty dietary characterized by the excessive consumption of foods rich in animal albumen and poor in food salts.

With this fundamental understanding of the disorder it follows that the necessary steps to be taken include: (1), elimination; (2), alkalization; (3), restoration of normal digestion; (4), restoration of metabolic function.

1. Elimination: The following treatment is outlined by Guelpa: For three or four days all food is suspended and from 1 to 1½ ounces of sodium sulphate or sodium phosphate dissolved in hot water is administered daily. Guelpa emphasizes the importance of taking the saline purgative warm. Tea or coffee, with a little sugar, are allowed and water may be consumed freely. This may seem a hardship to many people but the physician may assure the patient that if the purging be carried out effectively little or no suffering will result. When the disease is complicated with nephritis the patient should use castor oil, senna or some other suitable cathartic daily in place of the saline. The fasting period is followed by a milk diet for three or four days, two or three pints being taken daily. Koumyss or buttermilk may be substituted for sweet milk. The milk should be sipped slowly. Repeat the purging and fasting. A diet may now be adopted consisting of: Breakfast—vegetable soup or fruit, with coffee or tea with a small amount of sugar. Lunch—salad, fruits, two ounces of potatoes or one

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ounce of whole wheat bread. Dinner—same as lunch, except that the salad is replaced by vegetable soup.

After each meal two tablets of Trypsogen should be taken and the daily amount increased by 1 tablet per day. After this regime has been kept up for one week, it should be followed by three days of fasting and purgation, as before, and then a richer vegetable diet, with increasing quantities of bread and potatoes, is allowed. The dose of Trypsogen should then be gradually increased until the patient is taking 5, 6 or even 7 tablets after each meal.

The sugar will disappear in most cases, but will return in a diminished quantity on the resumption of food, and diminish progressively after every fast. Even after a thorough course of this treatment the patient should be admonished to take a course of fasting and purging, as outlined above every month, until the physician is satisfied with the success of the elimination process. Where albumen is present or where there is a distinct tendency to edema, *Trypsogen without gold and arsenic* should be employed. In some cases it will be found desirable to have half the dose consist of the ordinary Trypsogen, and the other half of Trypsogen Without Gold and Arsenic.

2. Alkalization: It is desirable that the blood and tissues of the diabetic should be restored to something like normal alkalinity and for this purpose the enteric coated Alkaline Pill (G. W. C. Co.) is recommended. This pill contains salts of sodium, potassium and calcium and is intended to dissolve only in the duodenum. At first two of these pills should be taken every hour during the day until it can be determined that alkalization has been accomplished. This is easily done with the litmus paper test of the urine and feces. A mixture of two ounces of bicarbonate of soda with one ounce of bicarbonate of potash may also be used at night when the patient arises to urinate, as the stomach is then at rest. A level teaspoonful of this should be taken dissolved in a tumblerful of water. With the combined use of the alkalies and Trypsogen, it will be found that in the majority of cases the subalkaline condition can be restored to normal.

3. Restoration of Normal Digestion: There is no mistake in selecting the gastrointestinal tract as a field for therapeutic attack in diabetes. Insufficiency of ferment action, as it relates to fat and protein digestion is the rule in most cases. In Trypsogen the proteolytic and lipolytic ferments predominate and a more thorough digestion of these food elements is thus insured. This is evidenced by the lessened

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bulk of the stools and their freedom from fat. The patient will experience a sense of comfort after taking Trypsogen and a lessened formation of gas owing to diminished intestinal putrefaction. The improved nutrition and the inhibition of the production of toxins will greatly favor his sense of well-being. Should intestinal putrefaction and constipation prove unduly persistent the patient should take two or three Secretogen Tablets before each meal.

4. Restoration of Metabolic Function: Since diabetes is a condition in which the power to burn sugar in the tissues is lost to a greater or less extent, endeavor must be made to develop the patient's metabolism so that he will be enabled to oxidize sugar in greater measure, even though he may never obtain the level reached by the normal individual. The raising of the alkalinity and the improvement in intestinal indigestion will increase to some extent the tolerance for starch food, and Trypsogen, by virtue of its contained internal secretion principle of the pancreas and by reason of the bromides of gold and arsenic which depress adrenal function, will materially assist in developing this tolerance for carbohydrates. At the same time it is well not to form the idea that there is a fixed quantity of carbohydrate which the patient can take care of. The quantity will vary from time to time but, under persistent and systematic treatment with Trypsogen and the Alkaline Pill, it will become larger and larger in the majority of cases.

Following the establishment of something like a normal condition the following suggestions as to a dietary will be found serviceable. Breakfast—one pint of milk, koumyss or buttermilk; fresh fruit according to season; salads if possible and bread made from genuine whole wheat flour. Lunch—a green salad and two slices of whole wheat bread; or natural brown rice with milk or koumyss or buttermilk. Nuts and fruit may be added when advisable. Dinner—a chop or small steak or small portion of broiled, roasted or boiled meat. Green vegetables, cooked by steaming; the water which collects should be utilized for the preparation of sauces or soups. Green salads may take the place of the steamed vegetables. For dessert some ripe fruit, or salad and cheese may be eaten.

The above dietary is only suggestive and may be modified at the discretion of the physician. Animal food should be used very sparingly as it is known that animal protein acts as a whip to the sugar-releasing mechanism of the liver with a consequent increase of the glycosuria. Eggs, milk and cheese are better suited to the needs of the diabetic than flesh meats, and if the latter are used mutton and chicken are preferable. Fish such as haddock or cod are better than salmon, herring and heavier fish foods. Fats, oils and rich gravies should be used cautiously, lest they upset the digestion and increase the acidosis. The kind of fat used must be determined by the patient's ability to digest it. Bacon, fresh unsalted butter, and yolk of egg are among the best of the fatty foods. Olive oil may be used sparingly on salads, the vinegar being replaced by lemon juice. In the case of carbohydrate foods, the various cereals are tolerated as a rule better than bread. Labbè classifies the carbohydrates in the order of their suitability: Potatoes, oatmeal, macaroni, rice, beans, peas, milk, bread and sugar. Potatoes should be steamed in their jackets or baked, and if baked the skin should be eaten also. The use of whiskey, brandy or light sour wine should be subject to the discretion of the physician. All sweet wines and beer are forbidden. especially beer. Exercise is allowable in mild, forbidden in severe cases, and out-door sleeping is almost as serviceable to the diabetic as to the consumptive.

DIABETES IN CHILDREN.

It is usually claimed that diabetes in children is much more fatal than in adults. Apart from any acute disease this greater fatality may be due to the old time starch-free dietary, and clinical reports which come to us bear out this statement, for Trypsogen is apparently as effective in children as in adults.

Diabetes has taken on a new aspect in the course of the last decade and while a strict carbohydrate-free diet in the adult is now regarded as very unwise, it is doubly so in children. Winters has shown that a grown child is always on the verge of an acidosis, because in its normal metabolism so much of the basic mineral substance is required.

Trypsogen with sensible dietetic treatment places in the hands of the physician an effective weapon in the treatment of juvenile diabetes. In the words of a very conservative New York pediatrist, who is looked upon by his colleagues as almost ultra judicial in the expression of an opinion: "There is not the slightest doubt in my mind as to the usefulness of Trypsogen in the treatment of young diabetics. I use it in every case and find it very serviceable." The opinion of this authority is well borne out by the numerous reports we have received from physicians in whose hands Trypsogen has proved itself of value in diabetes of children and adolescents.

Northampton, Mass.

Patient, a boy of 3 years. When first seen in March, 1908, he was very thin and sickly in appearance and hardly able to walk and was passing a large amount of urine heavily loaded with sugar. I put him on a strict diet with small doses of codein, but as he continued to lose strength I changed the treatment and prescribed Trypsogen. To my surprise there was a steady improvement from the first and in three months all sugar had disappeared. Treatment was kept up about eight months after this, the only article kept out of his diet being candy. He has remained well for two years, with no sugar in his urine, and is now in the best of health. No dietary restrictions during Trypsogen treatment or since. *Six years* later we received the following: The boy has been perfectly well ever since my last report and have not been able to find any trace of sugar in his urine. I keep up the use of Trypsogen tablets in my practice, but do not always get as good results as on this boy.

LOSS OF WEIGHT.

Loss of weight is one of the most common and most logical results of diabetes, and is one of the early and constant symptoms. It is also a symptom of serious import, and treatment should be directed toward an increase in weight and strength, which is often the first and best evidence of improvement. Trypsogen has produced very marked results in this respect.

Parkersburg, W. Va.

Patient, a married woman, 35 years, original weight 185 pounds; lost 35 pounds; high percentage of sugar; sp. gr. about 1032; much emaciated; sallow complexion; thirst, nervousness and pruritus. In four months, under the use of Trypsogen, 8 tablets t. i. d., the sugar has disappeared and normal weight regained. In fact, this patient now weighs a little more than normal and all symptoms have been cleared up.

DIABETIC GANGRENE.

The three principal factors at work which cause gangrene are: Alcohol, arterial changes and bacteria. Alcohol lessens tissue resistance, weakens the heart's action, and predisposes to arteriosclerosis. The severity of the arteriosclerosis and the virulence of the bacteria are the great determining factors. The idiopathic or dry gangrene is largely due to the changes in the arteries and veins; the altered metabolism plays but a predisposing role. By the introduction of bacteria from without dry gangrene is converted into an inflammatory or moist gangrene. How often this happens is shown by the fact that there are many more cases of the moist form. The comparative rarity of gangrene in women is less striking if we recollect how much less frequent arteriosclerosis and alcoholism are in women than in men. The improvement in nutrition following the use of Trypsogen helps to explain the benign effect in diabetic gangrene.

McKeesport, Pa.

I have used Trypsogen in several cases of diabetes and find it gives very remarkable results. The last case was complicated with gangrene in one foot, but after the use of Trypsogen for a few months the foot healed nicely and the patient has had no trouble since and is at his regular work. I assume Trypsogen effected the cure, as the patient had no other treatment, with the exception of some slight dietetic restrictions.

Batavia, N. Y.

Patient, a railroad engineer, age 48, normal weight 225 pounds. At the commencement of treatment weight was 175 pounds; urine of almost normal color; sp. gr. 1040; large amount of sugar; moderate polyuria. The chief trouble was gangrene of the little toe and portion of outer side of right foot, which required amputation. Under Trypsogen, healing rapidly occurred and patient's weight increased to normal. He is now at work apparently as well as ever.

SKIN COMPLICATIONS.

Not the least among the serious complications of diabetes are the pruritic conditions, the more serious infections of the skin and carbuncle. Resistance to infection is notoriously low in diabetes and surgeons hesitate to operate in these cases because healing is slow and sometimes impossible. We have a number of excellent reports which show that the regulation of metabolism made possible by this method of treatment favors the recuperative powers of the tissues and permits the healing of wounds, as well as skin lesions that have existed sometimes for many months.

Elgin, Ill.

Man aged 55, had had diabetes for several years and had been treated by a number of physicians. The sugar content was high and

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sp. gr. 1035. When he came to me I advised the use of Trypsogen and he responded promptly to it, an uncomfortable eczema and pruritus of the scrotum and legs disappearing very shortly. This patient made a complete recovery and there has been no return of the condition in the year that has passed since he finished the treatment. The highest quantity of Trypsogen that he took in a day was 21 tablets.

San Francisco, Cal.

Answering your query, I am glad to give you a brief report on a middle aged woman suffering from excessive pruritus and quite a serious abscess on her leg. Examination of the urine showed a large amount of sugar and it was obvious that she was diabetic and so I placed her on Trypsogen in increasing dosage. In a short time the skin troubles cleared up and the sugar disappeared. Two years later there was a recurrence of the same troubles and the woman went to another doctor who diagnosed the case as one of syphilis and prescribed iodine medication. The patient rapidly grew worse and, remembering what had been accomplished two years before, returned to me and was again placed on Trypsogen with the result that the sugar and the other symptoms disappeared and today she is practically free, but occasionally the analysis shows a slight trace.

ALBUMINURIA.

Albuminuria is probably the most frequent complication of diabetes. It has been noted in about 40% of cases. Toxic albuminuria is as a rule acute in its onset, manifesting itself at a terminal stage of the disease, either preceding or associated with diabetic coma. The renal changes are ascribed to the acetone and acid toxins circulating in the blood. While the albuminuria is never of a severe grade, it is in direct relationship to the increase or diminution of the acetone and acid toxins in the urine. The prognostic significance is grave.

The degenerative form is insidious in its manifestation. The renal irritation productive of this form arises from the action of the saccharine urine and prolonged hyperfunction and impairment of renal nutrition. While the appearance of albumin in this condition is of little immediate significance it is of eventual importance as indicating the complication of a chronic nephritis with existing diabetes. A matter of interest in connection with this form of albuminuria is the frequency disappearing and coma ceasing. She made a safe progress to full term and for the third time was delivered of a healthy child, since the birth of which she has enjoyed robust health without interruption or a recurrence of glycosuria attacks.

CONSTIPATION.

Secretogen tablets are probably the best means of combating constipation. They should be given in doses of two tablets half an hour before each meal and, if necessary, at bedtime. They not only excite secretion from the digestive glands, they have a direct action upon intestinal motility.

Trypsogen has been marketed for over twelve years, and its value has been very thoroughly demonstrated by the results which have attended its use in all parts of the English-speaking world. It has proved its value in over 60% of the cases treated. While it has never been claimed that Trypsogen will prove successful in all cases, it is probable that failure in some of the negative cases is due to insufficient dosage and lack of persistence in its use. When one appreciates the insidiousness of the onset of diabetes, and that it generally has back of it several years of development before the appearance of the well-known symptoms, the necessity for thorough treatment and large dosage of Trypsogen in obstinate cases will be evident. For this reason it is wise to prescribe a bottle of 500 or 1000 instead of 100.

DOSAGE: One or two tablets after each meal. The dose should be gradually increased until the patient is taking 5, 6 or 7 tablets after eating.

Trypsogen is put up in bottles of 100 (80 in Great Britain), 500 and 1000 five grain tablets.

Trypsogen *without gold and arsenic* should be specified as such.

Trypsogen is stocked by most jobbers and retailers in all English and Spanish speaking countries.

G. W. CARNRICK CO.

Manufacturers of Organotherapeutic Products

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A RECORD OF PROGRESS IN THE STUDY OF THE INTERNAL SECRETIONS AND METABOLISM

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The Metabolist

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Editorial

The old idea that tuberculosis begins with an initial infection with the bacillus and ends with its inevitable and triumphant march to the graveyard in the body of its host is giving way to a more rational view of the inherent resistance by the average human to this particular bacillary invasion. It is now known that about 90 per cent. of all cases that reach autopsy show healed lesions of the disease. This being so, resistance in the human must be at a high pitch and it is only when this resistance is at a comparatively low level that we have the tuberculosis diathesis, a condition that unless recognized and treated in time results in a favorable opportunity for the inroads of the germs and a consequent development of a full pathological clinical picture of the disease.

That a pluriglandular syndrome may be behind the tuberculosis diathesis is more than likely. Sajous says that to him the tuberculosis diathesis is a congenital or acquired insufficiency of the glands of the adrenal system. Sergent has described two forms of adrenal insufficiency occurring in tuberculosis. The first deals with the well-defined symptoms of Addison's disease, but it is to the second form—that of pulmonary tuberculosis—to which attention is particularly directed. As the disease progresses the symptoms of adrenal insufficiency become more marked. Sergent believes in Russell's theory that calcium starvation lies at the root of tuberculosis but calls attention to the experiments of Carnot and others who point out that the administration of suprarenal extract to an animal favors the deposition of calcium at the site of fractures. Halverson, Mohler and Bergheim in an interesting article on calcium in the blood in tuberculosis conclude that "the failure of the body to deposit lime around the tuberculous areas is to be attributed, not to a deficit in blood calcium, but rather to an inability of the cells of the tuberculous area properly to utilize all the available calcium." It might well follow that the caseation and calcification occurring in tuberculous foci in the lungs are due not merely to an increase of lime through the ingestion of suitable food but also to increased functional efficiency of the adrenal glands.

Toxemia is the usual cause of adrenal insufficiency and it is known that the presence of toxic material in the blood stream may result in either a hyper or a hypo-adrenia, depending on the amount of toxic material present and the degree of resistance offered by the adrenals in dealing with the toxic invasion. In tuberculosis it is evident that the amount of toxin is large and that the adrenals are inadequate to deal with it. This would indicate that treatment should be devoted not only to promoting adrenal efficiency but also to the inhibition of the formation of toxins. Attention is thus directed not only to the adrenals but to the liver and pancreas as well—two glands that undoubtedly show functional insufficiency in tuberculosis. Researches in the study of the disease show that certain lesions of the liver are in close relationship with it. Moreover it is evident that for long periods prior to the lesions functional hepatic insufficiency must have been present. Roubakin has worked on this phase of the subject and his conclusion is that virtually every subject shows evidences of such insufficiency. The stools show an absence of bile and it is not unreasonable to infer that the diarrhea of the consumptive may be due in some measure at least to disordered liver function. Further, Gilbert and Carnot point out that hepatic extracts have excellent coagulating properties and that they have employed them successfully in the treatment of hemoptysis in the third stage of tuberculosis when all other remedies have failed. Lereboullet has confirmed this and he has also seen good results with the extract in alcoholic tuberculosis patients with hepatic enlargements.

The pancreas, that very important organ of digestion, also shows signs of functional insufficiency in tuberculosis. Gray and Pickmann have demonstrated that pancreatic secretions are seriously diminished by toxins of tuberculosis in any stage of the disease and that persistently low trypsin readings of the stools are prognostically bad. But it is probable that the toxins of the bacillus are not the primary poisonous factors in producing tryptic insufficiency. The master toxin, as A. White Robertson calls it, in most cases is that produced by intestinal stasis. In his experience of vaccine therapy he has noted the failure of the organism to respond with an adequate supply of antibodies until the subversive primary toxemia is removed. Intestinal stasis is not necessarily a surgical condition and in the majority of cases it is probably due to a dilated duodenum with a consequent duodenal, hepatic and pancreatic insufficiency and incompetence of the ileo-cecal valve. Be that as it may, there is without a doubt a diminished pancreatic function and therefore diminution of enzyme action. Lewis, in *American Medicine,* (August 12, 1905), says: "Tuberculosis, the disease, is a germ disease. This is irrefutable, but its presence in human beings always implies that it is simply grafted on to some previous or pre-existing process favorable to its growth. Just what this process or condition is, still remains an open question, but there are substantial reasons for believing that a failure of proper metabolism provides the conditions essential for the development of tuberculosis. In order to establish a basis for a working hypothesis, I have not only carefully studied the literature of metabolistic phenomena, but have experimented as extensively and thoroughly as my limited time and facilities would allow. As a result of this study and investigation, which have been of absorbing interest, I feel more certain than ever that human susceptibility to tuberculosis consists primarily of a break or perversion somewhere in the sequence of enzyme action."

The *Medical Record* in an editorial says, "The future may witness the routine use of pancreas in tuberculosis, affections of the internal secretions (in addition to diabetes), and in many chronic affections with lowered opsonic index. Strubell, of Dresden, has shown that the administration of pancreas extract in tablet form increases the opsonic index to the staphylococcus, adding that extract of pancreas contains a substance which is concerned in the defences of the body."

Brieger draws attention to the power of pancreas to lower the antitryptic index of the blood in tuberculosis, and predicts a combination of tuberculin with pancreas extract as the eventual treatment of that disease. In this connection it is noteworthy to point out that in an article on the tuberculosis problem in the *Journal of the A. M. A.*, March 21, 1914, the writer says that it has been shown that the toxic substance of the tubercle bacilli may not be destroyed by pepsin but may be destroyed by trypsin. Thus the evidence that pancreas extracts are indicated in the treatment of tuberculosis is overwhelming.

Spleen extract has been used by Bayle in the treatment of tuberculosis and he says that the spleen produces substances—termed by him colloidogens—which hinder demineralization by maintaining the minerals of the blood in a colloidal state. To Bayle tuberculosis is a splenic insufficiency which in turn leads to demineralization, thus promoting a localization of the infection and creating a tuberculous area.

The use of thyroid preparations in tuberculosis is still the subject of much discussion, but it can hardly be questioned that in small doses the use of it is attended with benefit. Sajous has pointed out that thyroid substance is often used in ridiculously large dosage. If given in very small doses, it stimulates the glands of the adrenal system and has a tendency to increase blood pressure. There can be no question of its usefulness especially if combined with pituitary substance. Lereboullett says that the latter tends distinctly to raise the blood pressure and that it also seems to lower the cardiac rate, improve the appetite, promote sleep and benefit the general condition.

Organotherapy, not only on theoretical grounds, but in practical application, has justified its use in the treatment of tuberculosis and although these gland preparations may not possess directly anti-tuberculous properties, they not only serve to make up for insufficiency of the various organs coming under the baleful influence of the tuberculous infection reenforcing their action and assisting the organism in its fight against the disease, they also stimulate the corresponding organs to increased activity to relieve the symptoms themselves, and often to regulate the functions of various other organs, reducing their action when it is excessive and enhancing it when they show evidence of hypo-function.

As a medicinal adjuvant to the hygienic treatment of tuberculosis, organotherapeutic agents intelligently used hold the first place.

Professor Boas, writing for the *Berliner Klinische Wochenschrift,* says that after nearly two years of war the decreased consumption of food among the German people is responsible for the decrease of diabetes. Rather strong evidence that good-living, or over-eating is a large factor in the causation of diabetes.

Contemporary Comment

THE FUTURE OF THE INTERNAL SECRETIONS.

(This editorial by Dr. C. E. de M. Sajous is taken from *Endocrinology*. No one is more competent than Dr. Sajous to speculate on the future of the endocrine glands and the therapeutic possibilities that lie in directing and controlling the physiologic defenses of the body. His monumental work, "The Internal Secretions and Principles of Medicine," has gone through seven editions and it is not too much to say that Dr. Sajous has done more to stimulate the minds of physicians to a study of the internal secretions than any one else in the English speaking world.)

The leading feature concerning the internal secretions which still lurks in the minds of most medical men is one that will ultimately, in all likelihood, prove to be the least important, viz., organotherapy. Granting the far-reaching powers of the latter, when judiciously employed, and also the possibility that when organic agents will provide the actual physiological product of each gland the results obtained will far outstrip those now attainable; granting even that, as we have held, organotherapy may influence favorably some evil trends of heredity and react thereby against Nature's dastardly crime of "visiting the iniquity of the fathers upon the children unto the third and fourth generation"—eventually it will compare about as the moon does to the sun with the role of the ductless glands in the very life process itself and in disease. . . .

It will soon be fourteen years since the writer earnestly urged the American profession to devote some thought to this vast field, suggesting what appeared to him as fruitful avenues in the light of all the evidence then available and what personal observations, experimental and clinical, he could contribute. Time has shown that either through a happy concurrence of ideas, the teachings of experimental and clinical experience, or as offshoots, perhaps, of some of the seeds we had planted, many of the deductions therein set forth had a solid foundation. So distinctly has the trend of events sustained many of them that it were vain to deny to-day that when Swale Vincent wrote some years ago: "Sajous apparently postulates a relationship between all the ductless glands whose functions dominate most of the bodily activities, normal and pathological," he succinctly expressed the germ idea of what in the writer's belief, the future would demonstrate. Already it is beginning to appear that the progress of Medicine as a whole has been handicapped through the non-recognition of these structures which steadily are asserting their right to be classed with major organs, the heart, lungs, liver, etc., upon which all our labors have so far reposed. Their absence has seemed especially obscuring precisely where our role as physicians has demanded the greatest light, e. g., the pathogenesis of disease and the resources of the body to stay and offset its ravages.

In the great fields of neurology and psychiatry, to which work beyond computation and praise has been devoted, discouragement has remained the dominant note precisely where efforts on behalf of sufferers should have proved most telling. Nowhere has therapeutics remained less efficient. Indeed the growing proportion of feeble-minded and insane to the population attests to our inability to stem the tide. And yet, no single line of medical thought offers greater opportunity for development through the intermediary of the ductless glands. It may be recalled that we have long held that, in keeping with all other organs, the nerve-cell was a structure endowed with its own circulation, and that on the basis of methylene blue injections, the adrenal secretion, converted into an oxidizing ferment which was termed adrenoxidase, ascended the axis cylinder as tetano-toxin is known to do. Lichtwitz (1907-1908) likewise claimed the presence of adrenalin in nerves, though on vulnerable experimental evidence, as shown by Meltzer (1908); recently (1913), however, Macallum and J. B. Collop, obviously unaware of the foregoing labors, also referred to a "new substance in nerve cells," particularly in sympathetic cells, which they deem "allied to adrenalin."

If the circulation of the nerve cell proves as real as present indications seem to suggest, it would open an era of inquiry and development in the neurological and psychiatric fields similar to that which followed Harvey's discovery of the circulation in the grosser tissues, for biological chemistry and histology have made possible in our time what for him was beyond reach. Indeed, with their aid Nature herself seems to prod us to see the truth by a multitude of examples. Even red blood may be found in the nerve ganglia of Aphrodite aculeata, a sea annelid, while the ganglia of certain Nemertine worms contain hemoglobin with red corpuscles. Briefly, if what the writer believes proves true, we must entertain the thought that colorless blood devoid of red corpuscles, the sole oxygenizing fluid in many lower forms, is as active in our nerve-cells (and other cellular elements, muscular, dental, etc.) as is the red blood which so far has captivated our thoughts. If to this oxidizing body other components of the tissues at large are also found in the nerve-cell—as ample evidence is already available to show—we cannot but hope eventually to understand morbid changes which at present can only be described. Psychiatrists will then be able to do better than declare, as in a recent text-book, that "as is true of mania, there is no known pathology for melancholia," a sentence which applies to practically the whole gamut of mental diseases. Such a development cannot but greatly enhance their therapeutic efficiency.

It is not alone the adrenal product, however, which sustains metabolism. From 1903 to 1907 we submitted evidence in support of our opinion that it did so in conjunction with the thyroid secretion (first associated with metabolism by Schiff), a trypsin-like ferment and nucleoproteids, all distributed to tissue cells through the intermediary of leucocytes. Abderhalden (1905-1914) has independently reached very similar conclusions: "Everything points," says this observer, "to the fact that the [tissue] cell has agents at its disposal which render it capable of splitting up into their simplest units all the complicated substances which are brought to it or which it itself builds up." Again, "each separate cell, with very few exceptions, disposes of the same or similar ferments as those secreted by the digestive glands in the intestinal canal,"—those, as is well known, of the pancreas. As to the manner in which the tissue-cells are reached by these ferments, he writes: "Many facts accord with the suggestion that the leucocytes play a part in this connection." In keeping with what the writer had also held concerning the trypsin-like ferment, viz., that its proteolytic property was also the factor to which the phagocytes and the plasma owed their bactericidal and antitoxic activity, Abderhalden termed "defensive ferment" the digestive agent or agents referred to above, thus bringing "the so-called reactions of immunity into close line with processes that are normal and consequently familiar to the cells." Briefly, in keeping with what a deeper scrutiny of her methods seems to suggest, Nature, always economical in her ways and means, employs the same agencies (1) to prepare food stuffs for assimilation, (2) to convert the food and tissue wastes into eliminable end-products, and (3) to break down pathogenic substances and organisms to convert them likewise into eliminable end-products.

If the full meaning of these few facts is apprehended, it will be seen that probably we have in the ductless glands a foundation for the solution of many questions which, though studied with utmost diligence by a host of able workers during the last seventy years, have not as yet found their solution. Indeed, experimental and clinical facts tend increasingly to show that our inability to stay death in many diseases is due to our ignorance of the role of the ductless glands in these morbid processes.

All this applies as well to another tenebrous branch, therapeutics. On a Mediterranean-transatlantic liner, some years ago, diphtheria reigned supreme in the sense that the antitoxin on board seemed to have lost its efficiency—owing probably to deficient reactive powers on the part of the obviously debilitated immigrant children affected. Night after night a child or two was buried at sea. In despair the ship surgeon sought our aid, and we suggested that calomel be given orally besides the injections of antitoxin. The burials promptly ceased. The ductless glands had reacted and poured into the blood autoantitoxin which, added to the exogenous antitoxin injected, won the day. Millions of such examples are available in the practice of our professional fathers who used calomel indiscriminately—so indiscriminately, in fact, that on the plea that since small doses did so much good, large doses should do more good, they steadily increased the dose, salivated and debilitated—and finally killed the goose that laid the golden egg. The writer has long urged the powerful stimulating action of mercury upon the thyroid and adrenals and its remarkable property of stimulating actively through them the defensive functions of the body, mercury thus becoming what might be termed a thyro-adrenal stimulant, and also its pernicious influence in large doses on these glands.

Again, as is well known, digitalis, strophanthus and other agents of the same class, are supposed to owe their main beneficial influence to a direct action upon the heart. But we have long urged (1907) that these agents were adrenal stimulants and that their beneficial effects were due to this fact. Were it otherwise, why should Bezold and Boehm (1872) have arrested the action of digitalis by dividing the spinal cord and A. N. Richards and W. G. Wood (1915) have observed a similar inhibitive influence on the action of strophanthin and digitoxin by severing the splanchnic which is known to contain the secretory nerves to the adrenals? It has been shown also by Bedart and Mabille (1898) and confirmed by Ewald, Macaggi and others, that we could control overactivity of the thyroid and its untoward effects by means of arsenic. We thus have in this metal a thyroid inhibitant, a term which might be applied to other remedies.

These few examples, to which many could be added, will suffice to show that, irrespective of agents such as alcohol, phosphorus, ergot, ether, etc., which only incidentally affect the ductless glands, there is a vast field of study available through which we may, perhaps, eventually learn to develop the main object which therapeutics should fulfill—that of directing and controlling the defensive resources of the body.

Is there not ground for the hope that the internal secretions may thus fundamentally revolutionize medicine precisely where its needs are greatest, i. e., in the practical field?

SOME PHASES OF ACIDOSIS.*

Acidosis is now held to include a good many conditions which formerly were not classified under this head, and in fact it is now believed that acidosis plays a part, sometimes predominant, in the causation, or rather the progress of various diseases and affections. Within the past few years the question has been studied minutely and from several standpoints, and our knowledge in this direction has increased very considerably. Of those who have contributed to the attainment of this knowledge none has been more earnest in his endeavors nor more successful in his results than Cammidge, and it is therefore of interest to find his most recent views on this subject in the special acidosis number of *American Medicine* for June.

Cammidge defined acidosis as a condition in which there is an accumulation of acid products of metabolism in the body owing to an excessive production, or to defective elimination, or to both together, and he goes on to say that it is now generally agreed that the clinical symptoms of acidosis are not dependent upon any specific toxic properties possessed by these metabolic products, but arise from the impoverishment of the body in bases that occurs as a result of the acid character of these products. Thus, considered from the standpoint of a deficiency of bases, the term acidosis may be extended to include conditions in

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***Medical Record*, July 29, 1916.

which there is an excessive primary loss of bases, or an inadequate absorption of base-forming substances through the intestinal mucosa to meet the ordinary requirements of the body.

Consequently the possible causes of an absolute or relative acidosis are numerous and to a greater or lesser extent are encountered in a wide variety of conditions. Cammidge confines himself to a consideration of diabetes mellitus in which acidosis assumes the dominant rôle and is often the determining factor in a fatal issue. It is impossible in limited space to recount at length Cammidge's interpretation of acidosis in diabetes mellitus, and it must suffice to say that he points out that as a result of clinical experience a vegetable diet has come to be an important feature of most modern methods of treating diabetes, and that casein has been employed empirically in recent years as the chief constituent of many so-called "diabetic" breads, and biscuits. He further points out that a vegetable diet, or at least a system of dieting that contains a large proportion of "vegetable days," has other advantages, not the least of which is the preponderance of base-forming over acid-forming elements that it furnishes.

In the same journal a good deal of attention is paid to that condition of childhood known as cyclic vomiting. Eric Pritchard discusses this phase of acidosis in an original manner, and among the conclusions at which he arrives are that the measure of the severity of an acidosis is not to be estimated on the basis of the amount of acetone or other acid bodies in the urine, but on the degree of carbonate depletion, and that one of the effects on the system is to cause a serious hemolysis. Hence there must be an active regeneration of red blood corpuscles or a profound anemia will result. This is probably the explanation of the enlarged ends of long bones in rickets.

The more chronic effects of acidosis are observed in rickets, cyclic vomiting, recurrent bilious attacks, and the troubles connected with dentition. The treatment, both preventive and remedial, consists in the adjustment of the food to the physiological requirements in each individual case, combined with the administration of alkalies as may be indicated.

There is little doubt that our knowledge of acidosis is very much clearer than formerly, but it may also be said, without much fear of contradiction, that there is yet much to be learned on the subject. While we may be well on the way, we are by no means at our journey's end.

Articles of Interest

THE WHITE ADRENAL LINE: ITS PRODUCTION AND DIAGNOSTIC SIGNIFICANCE.*

By Emile Sergent, M. D., Paris, France.

Physician to the Charité Hospital.

When during the study of a case of adrenal insufficiency I accidentally discovered the vaso-motor phenomenon to which I gave the name "ligne blanche surrenale," I indicated in my first communication on this subject the method of bringing about this phenomenon.

Little by little, I have defined the various possible causes of error, figuring them out myself or noticing them in the reports of other authors.

It is necessary to follow certain rules which I shall now outline, for only those white lines can be considered as examples of the adrenal line which appear under conditions of technical research similar to those previously indicated, and which present characteristics parallel to those which I have assigned to this particular manifestation.

To bring about this phenomenon the skin of the abdomen is selected by preference and on it is traced a geometrical figure—a rectangle, triangle, or cross—thus obviating any possible confusion with lines possibly caused by scars, folds of the skin, etc. Ordinarily I outline a square around the umbilicus with a blunt object, as the rounded end of a fountain pen or, simply, the finger tip, taking special care to avoid rubbing, particularly with the nail. The figure should be made by a simple superficial stroking, one must neither bear down nor scratch. The motion should be deliberate and never rapid. The early or premature appearance of an outline is always a sign of clumsiness, as such treatment strikes and surprises the vaso-motors, thus interfering with the reaction instead of causing it. I am in the habit of telling my students that such a procedure is likely to be a source of error.

When the tracing has been made properly, all movement on the part of the patient is prohibited and one waits a short time. Immediately following the outlining nothing is seen, provided the proper technique has been followed; but after a few seconds, about half a minute,

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**Endocrinology*, January, 1917.

a pale line or band begins to be noticed following the course of the finger (or pen). Gradually this becomes more and more distinct and white, at the same time becoming larger, so that eventually the line exceeds in size the actual area touched by the finger tip.

This white line attains its maximum clearness in the course of about one minute, and persists for one, two or even three minutes before being gradually obliterated. This, at least, is what is to be expected in well-defined cases of adrenal insufficiency, the only ones, in fact, in which the test has any real value.

Certain errors may and do result from improper technique. I need only mention those due to an improper degree of pressure exercised at the time of making the tracing; but I wish to direct attention to some causes of error which may be due to various insignificant circumstances.

Naturally the lighting plays an important part. In bright daylight or sunlight, or even in bright electric light, it is sometimes difficult to see the white line. It is my custom after having made the tracing, to draw up the sheet or clothing in such a way as to cast a light shadow such as may be produced by a screen. By taking this precaution, I have demonstrated the phenomenon perfectly when a test made just before had failed to disclose it.

In like manner all factors causing a direct or indirect influence on the capillary circulation of the skin of the abdomen may modify the vaso-motor reactivity and, therefore, disturb the conditions favorable to the test. Hence it is useless to seek the line in a subject whose abdomen previous to the test was covered with a poultice, fomentation or compress. A number of minutes should be allowed to elapse after the removal of such applications before making the test. Also in subjects who are clothed one should wait a while so that pressure from the corset or underclothes can have no influence. For that matter, in ambulant cases this local pressure influence is not the only deterrent factor to be looked after, the upright position, fatigue and the effects of walking all have a certain unfavorable influence. In a word, if you desire to follow the exact technique, before making the test place the patient at rest for at least fifteen minutes with the abdomen free and but lightly covered.

It seems advisable not merely to outline the rules of technique, but to emphasize the objective characteristics of the "ligne blanche surrenale," so that it may not be confounded with other vaso-motor condi-

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tions from which it must be distinguished. The phenomenon which I originally described must be differentiated from certain white lines accompanied by red lines appearing simultaneously, encircling them or being encircled by them, and preceding or following them. In this connection there will be found in a recent communication by Ravaut and Kronatlinshl read before the Société Médicale des Hopitaux here in Paris, a detailed study of these various lines.

The diagnostic significance which I have deduced from my researches is concerned solely with white lines presenting the characteristics repeatedly and accurately outlined by me—to the white line which I have called "adrenal." In attributing to this a pathogenic quality I have considered it purely as a symptom of adrenal insufficiency. To my way of thinking it is a result of hypotension brought about by the hypoadrenia. To understand the philosophy of its production by such light stroking I have proposed the following explanation: In arterial hypotension we know that there is a peripheral vasodilation; if we begin to produce a light stimulation of the skin, vasoconstriction will replace the vaso-dilation.

I will not discuss here the objections which have been brought up—I have done it before and quite often enough. But I will reiterate some general considerations which have been previously presented by me. In pathology as well as in clinical medicine there are no pathognomonic symptoms, in the absolute sense of the term. Diseases are recognized by the presence of a group of symptoms, and these symptoms of the same disease do not necessarily show themselves in exactly the same manner in every case, for here a certain symptom may be absent, and there another. However, some symptoms are more constant and consequently of greater value than others, and this is the case with the white line in the syndrome of adrenal insufficiency.

Is it, then, sufficient ground upon which to base a diagnosis? To answer this definitely would be exceeding the scope of this paper, and going a little too far. As I have said before, and as I maintain, when I determine the presence of the "ligne blanche surrenale," my attention is quickened and immediately I begin to look for the other signs of hypoadrenia, such as melanoderma of the Addisonian type which, in turn, causes me to look for other evidences of Addison's disease. This does not necessarily prove that the melanoderma cannot be present save in a typical Addison.

Again, rose spots have a symptomatic value conceded by all clinicians in the diagnosis of typhoid fever. Does this mean that typhoid cannot exist without being accompanied by these rose spots, or that these same spots cannot be found in other diseases than typhoid? Are all tachycardias necessarily of thyroid origin? Nevertheless does not the discovery of tachycardia stimulate us to look for other symptoms of the Basedow syndrome?

I wish here to warn the profession against a somewhat growing tendency to seek the absolute in clinical medicine. The clinic only permits an approximation; possessing neither an absolute sign of value, nor an incontestable diagnostic measure; but it strives rather to group signs and syndromes and to associate with them the results of functional action and reaction.

It is only with such ideas in mind that we should seek to demonstrate the "ligne blanche surrenale," and that we will be able to appreciate its diagnostic value.

A CASE OF ASPERMIA.*

By Seelye W. Little, M. D., Rochester, N. Y.

This case is reported because it shows the possibility of successful treatment based upon what a few years ago was totally unknown and at present is known only fragmentarily and in a general way—the function of the ductless glands.

E. B., school teacher, aged 32, married six years; no children.

Being very intelligent, and greatly desiring to have children, he consulted a very competent specialist in genito-urinary disorders. This physician could find absolutely nothing to account for the aspermia which was present. Repeated examinations of condom specimens over a period of several months failed to reveal a single spermatozoon. A vas deferens was finally tapped near the epididymis and a sample of testicular secretion for examination was obtained. This too contained no spermatozoa. Gonorrhea, syphilis and exposure to X-ray could be absolutely ruled out. Sexual feeling and coitus normal. Patient sent tc writer with a view to possible ductless gland therapy. Family and personal history irrelevant except possibly the fact that patient resembles mother, whose mother died of an ovarian "tumor."

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*_Boston Medical and Surgical Jour._, March 8, 1917,

Patient a man of average size and build. Very well balanced mentally. Skin, normal. Hair, normal on head but very abundant on arms, legs, chest, abdomen and pubes. Heart and lungs, normal. Urine, normal. Teeth, doubtful. Gums, tender and bleed easily. Appetite, good. Bowels, tendency to constipation. Sleep, normal. Penis very large for size of man. Testicles large.

From the data it would appear that the man is on the whole about an average male. By a process of exclusion it was decided that the cells from which spermatozoa develop were probably present but dormant. We know that some of the ductless glands have a great influence on the growth and development of the generative apparatus. These glands are especially the thyroid, the pituitary and the suprarenal *cortex*. Furthermore in this case if the fault lay in any of the ductless glands, obviously it must be a case of hypo-function.

There were no symptoms of hypo-thyroidism, such as myxœdema, even in slight degree. The pituitary was ruled out also for lack of symptoms such as polyuria, drowsiness, lack of ambition, obesity, low blood pressure and the like. On the other hand two facts pointed to a former hyper-action of the suprarenal cortex—the body hairiness and large size of the external genitalia. Hyper-action of any organ implies eventual hypo-action of that organ. Accordingly we acted upon the theory that this patient for an indefinite time, probably from some time after puberty, had had a condition of cortical hyper-suprarenalism.

He was given 4 grains of dried suprarenal cortex daily, increasing to 6 grains daily. Treatment was begun on Sept. 23rd. On Nov. 25th a few perfectly formed spermatozoa were found in a condom specimen. The finding was confirmed by Dr. M. L. Casey, pathologist to St. Mary's and the General Hospital.

Sensitiveness to Epinephrin in Dementia Precox.—(W. Schmidt, *Münchener medizinische Wochenschrift*). Cases of dementia precox, especially the catatonic and hebephrenic forms, are not sensitive to injections of epinephrin, i. e., the blood pressure does not seem to be affected. Normal individuals, as well as those affected with other psychoses, react to the subcutaneous administration of epinephrin by a marked increase in blood-pressure.

Brief Abstracts

Insanity and Amenorrhea.—(J. W. Dunbar Hooper, *Australian Medical Journal*). A patient, when seen 21 years old, was anemic and constipated, and had suffered from melancholia for three years, during which time she had menstruated twice only, very scantily and with great pain. After more than twelve months of treatment, which included curetting, she was placed in an institution, where she spent a year. She was then found to be suffering from religious mania with amenorrhea, was occasionally vicious, and at such times refused food. It was decided to remove an ovary and to substitute for it a more normal organ taken from a sane person. A hysterectomy upon another patient provided the required material, which after removal was placed in Ringer's solution at blood heat. Four and a half hours later the abdomen of the insane woman was opened. Both ovaries were very small, hard, pale and cirrhotic. The more abnormal of the two was removed, the broad ligament on that side split, and the new ovary, cut into three slices, was imbedded in the nest thus provided. Recovery was uneventful, and twenty-four days after the operation a normal, painless, profuse menstruation took place. The mental condition improved rapidly, and in six months the patient was dismissed to her home. She was then menstruating regularly, had put on 6 pounds in weight, and was exceptionally bright and happy. She declared her intention of doing her utmost to repay her parents for the trouble and expense of her treatment; in a word, her insanity had entirely vanished.

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Protective Action of the Adrenal Glands.—(W. B. Cannon, *American Journal of Physiology*). Evidence goes to support strongly the view that the adrenal secretion can be brought into rapid and valuable action upon lines calculated to strengthen the individual against possible harm, and is similarly brought into play with the major forms of emotion. Its action consists of a shifting of the blood from the visceral parts to the skeletal; an enhanced force of the heart beat; an immobilization of the viscera; and, in particular, an increase of sugar supply to those structures most needing it. The shifting of the blood favors the fuller action of the skeletal elements upon which repulse of injury depends; this is gained at the temporary sacrifice of the viscera, which are immobilized; the more powerful cardiac action is affected by the peculiar action of the adrenal secretion upon the coronary arteries, for these are the only vessels which dilate instead of contract with the action of adrenal. Lastly, the increased ability of the tissues to metabolize sugar increases their power, and in the skeletal tissues this is, again, just what is wanted. The whole gamut of changes afford the spectacle of a most intimate and closely organized arrangement for the rapid focusing of added power to those structures most valuable for the immediate end in view, namely, the protection of the individual.

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Thyroid Insufficiency, Nervous Conditions, and Spastic Constipation in Women.—(Sehrt, *Münchener medizinische Wochenschrift.*) Report of 9 cases of nervous disturbance accompanying hemorrhagic uterine affections, ascribed to defective functioning of the thyroid and treated with thyroid extract; likewise 8 cases of nervous disturbance accompanying retarded development of the internal genitals. The benefit from thyroid treatment was constant and so marked that it can be explained only on the assumption that the neuralgias, vague pains and fatigue were due to excessive irritability of the nerve terminals which had gradually developed under the influence of protracted autointoxication from lack of thyroid function. Such autointoxication may be the direct result of the thyroid deficiency, or merely promoted and increased by it; in either event thyroid treatment has a distinct causal efficacy. For the detection of such thyroid insufficiency, the author suggests that a preliminary blood examination be made to determine if there is a significant relative neutrophile leucopenia with relative lymphocytosis. The action of iodothyrin in these cases is that of a regulator. Spastic constipation is to be considered the direct opposite of diarrheas observed in hyperthyroidism. Even when of years' standing, it is amenable to treatment.

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Thyroid Treatment of Uterine Hemorrhage.—(E. Sehrt, *Münchener medizinische Wochenschrift*). Attention called to the close connection between the hypophysis, thyroid, and genital organs. The connection between the thyroid and the ovaries seems to be particularly close, and the thyroid may be responsible for conditions in the ovaries which entail bleeding in the uterus. The characteristic behavior of the blood when the thyroid is functioning to excess or not enough may account for this. With hyperfunction, the blood is abnormally slow in coagulating; with deficient functioning it coagulates abnormally quickly. The author found in 55 cases of uterine hemorrhage without discoverable local cause that 38 of the patients had all the signs of pronounced hypofunction of the thyroid. On this basis he gave thyroid treatment and in every case marked benefit was apparent. Not only the hemorrhages, but the general health showed a decided change for the better. Complaints such as palpitation of the heart, headache, etc., were occasionally improved after the first few doses. Leucopenia disappears after a few weeks of medication. Hemorrhages cease or become normal even after medication has been discontinued, thus proving the causal relations of thyroid insufficiency and hemorrhagic metropathies.

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Pituitary Extract in Obstetrics.—(Lindeman, *American Journal of Obstetrics*). Where the cervix is not over four fingers dilated, the author gives only 0.05 Gm. of pituitrin. He never used more than 0.1 Gm. as an initial dose. If 0.2 or 0.4 Gm. be given and an extremely violent labor result, it is almost impossible to control the pains, even with chloroform. With cautious dosage the author has had no instances in which pituitrin brought about contractions of the uterus so powerful as to interfere with the placental circulation and cause deep asphyxiation of the child. In the induction of labor large doses—0.1 to 0.2 Gm.—may be given with perfect safety. It would seem that so much of the energy of the drug is used up in starting the labor that the pains induced are never very strong at the outset, the effect wearing off before stronger pains develop.

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Successful Epinephrin Treatment in Osteomalacia.— (Salis, *Münchener medizinische Wochenschrift*). Report of a case of recurring osteomalacia noteworthy because of the continuation of the disease in spite of castration 11 years before, and the energetic and prompt healing action of epinephrin. After 2 injection series of 9 injections each,—0.5 c. c. at a time—the symptoms disappeared and the patient was able to resume his duties. The improvement had continued several months after the treatment ceased.

Role of the Corpus Luteum in the Induction of Mammary Secretion.—(P. Bouin and P. Ancel, *Semaine médicale*). Experiments are reported as a result of which the authors conclude that, under normal conditions, the corpus luteum not only is the determining factor in the enlargement of the breast during pregnancy, but, in addition sensitizes the mammary cells to the action of another factor, which causes them to manifest their secretory function. This other factor must be in the nature of an internal secretion. Under certain experimental conditions, a uterine or parauterine mechanical stimulus is capable of exerting the same action as the specific hormone. The mammary gland only reacts, however, to this traumatic stimulation if it has been subjected to a sufficient degree of sensitization from the corpus luteum.

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Peripheral Action of Epinephrin, with Especial Reference to the Lungs.—(D. E. Jackson, *Journal of Pharmacology and Experimental Therapeutics*). The author was able to show conclusively that epinephrin produces a prompt dilatation of the bronchioles where these are contracted; this effect is wholly independent of the rise of blood-pressure. Injection of a small dose of pilocarpine into the spine of a dog with vaso-sympathetic nerves cut, produces a slight bronchoconstriction, which is soon followed by a moderate but usually prolonged dilatation; this latter change does not occur if the adrenals have been previously excised or clamped off, and may therefore be ascribed to stimulation of these glands or to an increased secretion of epinephrin. Nicotine causes, after brief initial constriction, a dilatation, which appears to be due to an increased secretion of epinephrin caused by the nicotine.

* * *

Pituitary Extract and the Stomach—(Houssay, *Semana Medica*). The author used an extract of the posterior lobe of the pituitary of the bullock prepared by boiling 1 part of the gland in 5 parts of water, precipitating the albumin with lead acetate, treating the excess of lead with sulphuric acid, and neutralizing. One c. c. in salt solution, injected subcutaneously, promoted the contractility and secretion of the stomach, while the tone and the rhythm were regulated. The results were both experimental and clinical. On the excised stomach a similar effect was produced.

Corpus Luteum Extract in Nausea of Pregnancy.—(John Cooke Hirst, *Jour. Amer. Med. Assoc.*). The author considers that there is a connection between the corpus luteum and the nausea of pregnancy, as the nausea begins to diminish at the time the corpus luteum has reached its acme of development. Acting on this idea, he has administered corpus luteum extract in doses of 1 c. c. (20 mg.) daily. This dose is probably too small, and he thinks it may be increased, but he had very successful results in four out of five cases in which it has been tried. The one failure shows that it cannot always be depended upon, but the results in the other cases are sufficiently encouraging to warrant further trial of the remedy.

* * *

Toxic Action of Pituitary Extract in the Newly Born.—(Sheffield, *American Journal of Obstetrics*). A new-born child, after nursing about twenty minutes, was gradually seized with recurrent attacks of muscular contracture. These subsided but reappeared with great severity after a feeding two hours later. As there were no other signs or symptoms to account for the spasms, which set in after the child took the mother's milk, and as the muscular contractures were tonic and at regular intervals, resembling uterine contractions, the author concludes that they were probably due to pituitary extract transmitted by the mother's milk. Breast feeding was stopped; the convulsions ceased very gradually within two days, and did not return thereafter.

* * *

Hypophysis Cerebri and Diabetes Insipidus.—(C. Römer, *Deutsche medizinische Wochenschrift*). After experimental investigation, the author denies that secretion of the pituitary gland produces polyuria. Upon injection of mercury into the base of the pituitary gland of rabbits, a markedly increased secretion of urine resulted. Injection of colloid extracts, i. e., extracts from the pars intermedia of the gland, produced no increase in the amount of urine excreted. In one case of diabetes insipidus, intramuscular injections of pituitary gland extract were followed by lessened excretion of urine and marked improvement. Autopsy revealed a tumor of the base of the brain involving the base and posterior lobe of the hypophysis.

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Civilization and Tuberculosis.—Knopf, (*Medical Record*, July 21, 1917, Vol. 92, No. 3), says that it is today universally admitted that the vast majority of the people who have lived for generations in cities and towns have at some time had a tuberculous infection. Modern pathological science corroborates this, for the majority of individuals who have died from accidents or other diseases than tuberculosis have shown, when their bodies were autopsied and all organs macroscopically and microscopically examined, that they had had a tuberculous infection at one time or other in their lives. Many authorities maintain that this infection even conveys a certain immunity to future infections and that only when a new invasion of tuberculosis germs becomes overwhelming, or when privation, malnutrition, exposure, intemperance, lack of air and sunlight, or overwork undermine the natural resistance does the latent tuberculous focus which was the result of the primary infection, suddenly become active and we have a tuberculous disease. In his research work he discovered that the age at which a tuberculous infection contracted in infancy or childhood usually becomes active is at or after 15 years. He says: "I can only account for this by the prevalence of child labor causing an excessive physical strain on the delicate growing organism which loses its natural resistance to a new invasion of the bacilli or the awakening of a latent infection. Child labor, which is still the curse of our nation in many states, is a factor of our modern civilization largely responsible for the high morbidity and mortality rate from tuberculosis among our young people, particularly at the period of adolescence. . . . Civilization, such as it is, is doubtlessly responsible for much if not for all the tuberculosis in existence. But there is still hope, for this same civilization has also awakened in man his sense of duty in the combat against the great white plague. In nearly all countries of Europe and America antituberculosis work has been in progress and our country has not been behind. In Europe the present war has not only, as already pointed out, increased the fearful morbidity and mortality of the disease, but it has also stopped all educational propaganda and all municipal and state philanthropic enterprises which were directed against tuberculous invasion. Let us hope that when the strife will at last be ended there will be a reawakening throughout the civilized world and a renewed activity of all the agencies which have been heretofore so helpful in the antituberculosis crusade. Civilization, such as it should be, can do away with this as

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well as other diseases of the masses. Tuberculosis can be prevented, it can be cured, it can even be eradicated by true civilization; but to be truly civilized, we must replace ignorance and superstition by education and enlightenment, social injustice by social justice, selfishness and greed by love and generosity, egotism by altruism."

* * *

The Function of the Adrenal Bodies.—Swale Vincent writing on this subject, (*Endocrinology*, April, 1917, Vol. I, No. 2), comes to the following conclusions:

1. What we call the adrenal body represents the anatomical association of two elements, each one of which is derived from a separate and independent system. The adrenal body proper or cortex is part of the "cortical" or "interrenal" system. The medulla is simply an accumulation of chromaphil cells of the same nature, histologically, chemically, and pharmacodynamically, as similar but smaller masses along the sympathetic at other levels.

2. There is no clear evidences that these two systems are functionally related to one another.

3. The adrenal medulla (as well as the "chromaphil tissue" generally) is derived from the sympathetic nervous system, and is alleged to facilitate this system's functions in certain physiological emergencies.

4. The cortex is derived from the germ epithelium and there is considerable evidence that it has important functions in connection with the development of the reproductive organs.

5. There is a considerable mass of clinical evidence that tumors of the adrenal cortex are frequently associated with sex abnormalities.

6. Additional evidence in the same direction is furnished by the enlargement of the cortex during breeding and pregnancy.

7. It is possible that a final solution of the problem as to the relation between the adrenal gland and sex will only be arrived at when the wider problem of the relationships between the various ductless glands shall have been solved.

8. Feeding young animals with adrenal gland substance seems to stimulate the growth of the testis.

9. The cortex is the part of the gland which is essential to life. We do not know why its removal causes death, but it is possible that this is due to some defect in muscular metabolism.

10. The symptoms of Addison's disease are in no way explained by the accumulated results of investigations in the comparative anatomy and the experimental physiology of the adrenal bodies.

11. It is too early to attempt to diagnose clinically any syndromata due to hyper- or hypo-function of the adrenal bodies.

* * *

The Sclerodermic Type of Pluriglandular Insufficiency.—(Reports of the Clinical Conferences of the Neurological Institute of New York, 1915). Walter Timme reports an interesting case of pluriglandular insufficiency in a woman 55 years of age who complained of weakness of the extremities and cramps of the calf muscles. Two years before she had had a stiff neck which caused a great deal of pain and the following year she noticed some difficulty in opening the mouth. Since then she had had increasing weakness of the extremities until she was unable to leave the bed. Examination revealed cyanosis of the extremities and a dry peeling condition of the skin. There was a symmetrical pustular eruption on the face, and the skin over the chest and neck showed a brownish discoloration. The hair was dry. The skin of the lower extremities showed areas of induration. The skin of the face had become indurated to an extent that interfered with the movements of the eyelids and of the mouth. The thyroid gland was somewhat enlarged, the urine and blood normal; Wasserman test negative. There was a marked amyotrophic condition of the arms, forearms and especially of the hands. Extension was impossible. There were also signs of progressive muscular dystrophy. Babinski reflex was absent. There was no ankle clonus. She could not sit upright without help and could not stand.

This case presented a complex pluriglandular insufficiency; the pigmentation indicated a suprarenal insufficiency; the dry and scaly skin indicated hypothyroidism. The amenorrhea, the paresthesias and cyanosis were due to ovarian insufficiency and, possibly, also to the suprarenal insufficiency.

The organotherapy indicated in this case was ovarian and thyroid extract. After three weeks' treatment the skin eruption disappeared, the discoloration faded, and the movements of the arms and legs improved,

Combined Bromide and Thyroid Treatment of Epilepsy.—(Sicard, *Journal de médicine de Paris*). The tendency to bromism may be combated by the administration of thyroid gland. The writer administers in a cachet 1½ grains (0.1 Gm.) of dried thyroid every morning for three weeks, suspending the administration from time to time for a fortnight. Two doses, each of 15 grains (1 Gm.), of potassium bromide are given daily at equal intervals from meals, say at 10 A. M. and 10 P. M., dissolved in half a wineglassful or less of water. The bromide is to be given regularly. A chlorine-free diet is enjoined, and, should acne appear, the pustules are to be treated with an application of chlorinated soda solution and sulphur ointment.

* * *

A Case of Family Acromegaly.—(*Med. klinik*, Nov. 14, 1915, p. 1267). After a description of two cases of acromegaly developing in first cousins, Leva gives a brief review of the pathological anatomy. After extirpation of the hypophysis in half-grown animals, we observe inhibition of the general growth, obesity, defective mobility, defective union of the epiphyses, an increase in the colloidal material of the thyroid, hypoplasia and degeneration of the genital organs. In acromegaly the anterior lobe of the pituitary gland plays a far greater role functionally than the posterior lobe of the hypophysis. Several authors have already called attention to the etiological importance of a neuropathic family history and of consanguinity. It is possible that a consanguinity plus the family history form a cumulative neuropathic irritation which culminates in the development of acromegaly.

* * *

Iodine Content of the Thyroid.—(Cameron, *Journal of Biological Chemistry*). The author found iodine in the thyroids of the pigeon, alligator, and frog, in amounts corresponding with the diets of these animals. It is also present in the thyroids of the dogfish. Thus, further support is given to the theory that iodine is an invariable constituent of thyroid tissue. The amount of iodine present in the parathyroids of the dog is of a less order of magnitude than that in the corresponding thyroids, if, indeed, the actual quantity observed be not wholly attributable to thyroid contamination. Such results indicate a differentiation of function between the thyroid and parathyroids.

KINAZYME IN TUBERCULOSIS.

Success in the treatment of tuberculosis depends solely on raising cell resistance. As lowered nutrition, through an insufficient ration or imperfect digestion or both, has been the means of rendering the cell susceptible to the invasion of the bacillus, our aim should be to supply the patient with the proper food in right quantity and also to enhance his digestive, bactericidal and antitoxic powers, until they reach a physiological standard. In a word our endeavor should be to restore to the cell the almost invulnerable armament of normal function. The cell does the rest; it will take care of the invader. No pathological secretion or principle, however cunningly applied, that is used solely with the purpose of killing the germs can ever "cure" the tuberculous patient. It can not take the place of the physiological secretion or principle that is the offspring of a cell that is normally nourished and which is the best safeguard against disease. As Dr. Leonard Williams says: "By the use of vaccine therapy we may repel an individual invasion, but we have done less than nothing so to fortify him (the patient) that out of his own resources he will in future be able to resist successfully similar onslaughts."

No serum administered for tuberculosis carries with it the physiological elements which will enable Nature to repair her shattered bulwarks; repair and recovery can come only through the organism itself. Sunshine, fresh air and a well-balanced ration constitute the first step in the successful treatment of tuberculosis.

As a rational therapeutic adjuvant to these hygienic measures the value of the extracts of certain animal glands has come to be recognized. Some three or four years ago we placed at the command of the medical profession under the name of Kinazyme, a combination of spleen, liver and pancreas with calcium. This preparation received much commendation but lately we have improved it by the addition of small doses of thyroid and pituitary extracts. That this addition has been well founded may be appreciated from the following letters received from the superintendents of two well-known public sanatoria for the treatment of tuberculosis:

> "Some time ago we received for trial some of your Kinazyme (Improved Formula) and we thought it helped some of our cases who were not doing well. It seemed to increase their appetite and made them feel more interested in life; two or three cases in particular seemed to improve under it. We want to continue using it and wish you would quote us a price on some and send us one dozen of the bottles."
>
> "I have used (Improved Formula) Kinazyme as prepared by you in my treatment of tuberculosis. I find it aids digestion and helps to relieve many of the cases of gastric distress and delayed digestion that occur in tuberculosis. It is also a material aid in assimilation and as nourishment is one of the cardinal necessities in the treatment of tuberculosis, I believe that you have a valuable product in your Kinazyme (Improved Formula)."

These gentlemen's opinions it will be seen apply to the Improved Kinazyme. Clinical reports on the old Kinazyme follow:

> "I wish to tell you of the patient suffering from tuberculosis for whom you sent me 500 Kinazyme Tablets. She was one of those down-and-out-nervous-prostration wrecks of females, with no appetite and ready to give up the ghost. On beginning the treatment I first gave her four tablets three times daily, later three tablets t. i. d., then two t. i. d. Her appetite improved from the start but the strength returned slowly. However, she now has a good appetite, has increased ten pounds, can go about without extreme fatigue and, whereas I considered the case hopeless, I now believe recovery will be complete, for all the soreness has left the chest, and expectoration has diminished and the cough has very much improved."
>
> "In reply to a letter received from you early in December last, I take pleasure in informing you that the sample of Kinazyme

Tablets which you sent me has been used on Miss ——, age 22, single, of American parentage, who has incipient pulmonary tuberculosis of the apex and base of the left lung following la grippe and acute bronchitis. The Kinazyme Tablets were given to the exclusion of all other medication except calcium sulphide gr. 1, t. i. d., p. c. The case shows a gradual and uninterrupted improvement. Her condition upon admission to the —— Hospital of this city may be learned from the following record: Temperature, 104.40F; pulse, 122; respirations, 40 per minute; she had an annoying cough, worse at night, with muco-purulent sputum which was "negative for T. B." on admission, but "positive for T. B." later. Physical signs of consolidation were present at the left apex, anterior and posterior, and also at the base of the lower lobe (left lung) in the infra-scapular region. The patient was given every advantage of Nature's triple cure, fresh air, rest and nourishment, but no other medication except as stated above. To show her case has improved, her evening temperature at 8 P. M. last night was 99.50, pulse 108, respirations 28. At 8 A. M. this morning her temperature was 98, pulse 96, respirations 28. She coughs very little during the night now, has no more night sweats, and her appetite is good. She is also gaining in weight."

"Enclosed find check for $4.00, for which please send me by return mail 500 of your Kinazyme Tablets; as you know I just ordered 100 and then 200 and the patient is feeling so much better he requested me to order 500 more for him. I am very thankful that we have found something that will benefit this man, or any other person that has tuberculosis."

"Replying to your inquiry of today I am delighted to inform you that your preparation Kinazyme which you have so generously supplied me for experiment has proved more than what you claim for it. I have a case on hand of a young man about 28 years old. He suffers with tuberculosis of the testicles. The disease has gradually spread to the bladder and to the inguinal glands. Finally he developed a systic hemorrhage. No treatment was of any avail and I have tried anything known to the medical profession but with no result. He was getting weaker and weaker from loss of blood and the glands grew in size, the testicles discharging through the scrotum profusely and peritonitis was staring in the face. I here decided to try your Kinazyme and after the first 24 hours administration the hemorrhage diminished and after one week's treatment the hemorrhage ceased completely, the glands became normal in size and the discharge greatly diminished; his general health marvellously improved. Is there anything more striking as an illustration of the value of your Kinazyme?"

Subsequent to the use of Kinazyme (Improved Formula) an immediate improvement is observed in the constructive metabolism of the body as shown by an increase in weight and strength. Kinazyme as a therapeutic adjuvant to the hygienic routine in tuberculosis gives most satisfactory results in the majority of cases. By its use a larger amount of food is digested and absorbed and the protective powers of the organism are greatly increased.

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The Metabolist

A RECORD OF PROGRESS IN THE STUDY OF THE INTERNAL SECRETIONS AND METABOLISM

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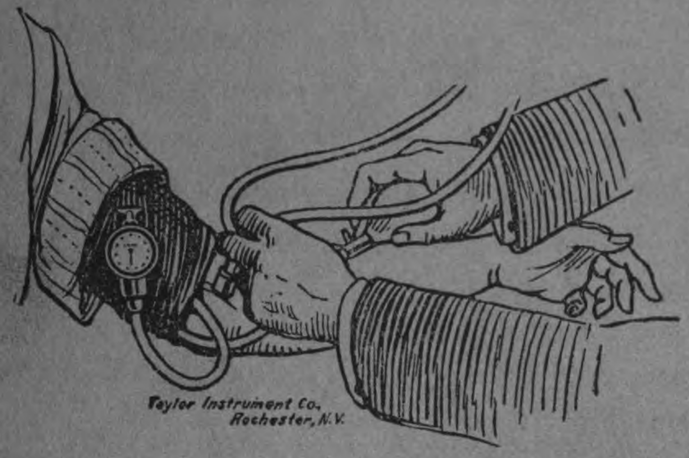

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RATIONAL TREATMENT OF HIGH BLOOD PRESSURE 62
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HIGH BLOOD PRESSURE NUMBER

The Metabolist

VOLUME THREE NUMBER THREE

Editorial

INCREASED RANK FOR ARMY DOCTORS.

It's a far cry from the days of Ambroise Paré, when the army surgeon was little better than a camp follower, to the present time when the military physician virtually holds the efficiency of an army in the hollow of his hand. Recognition of that fact is freely accorded by those in authority and this acknowledgment of his indispensability makes it all the more incomprehensible why there should be any opposition by the line officers of our military establishment to increased rank for the army surgeon.

Apart from any consideration of the increased danger now attending the duties of the average army doctor in a war of studied brutality on the part of our enemy, it must be admitted that the position of an army surgeon carries with it a responsibility second to none. Further, it should be recognized that most of the officers of higher rank in the Medical Reserve Corps have given up practices bringing them incomes immeasurably greater than they would ever receive in army life, and that they have done this in the most ungrudging spirit of unselfishness. Taken as a body, no branch of the army has shown a more unswerving devotion to their duty than the men of the Medical Reserve Corps.

It is to be hoped that there will be a cessation of the opposition on the part of the General Staff to the enactment of legislation that will accord to the army surgeon a full meed of the recognition to which he is justly entitled, not alone on the grounds of unalloyed patriotism but on the basis of the unsparing self-sacrifice he has shown in offering his services to his country in a critical hour. The physician who, for good and sufficient reasons, has felt that it was his duty to stay at home in

the present crisis should make his opinion felt on this matter and should write to his congressman and senators asking their support for this necessary and timely legislation.

"**High blood pressure** is a sentinel warning against renal and vascular degeneration." Time lost in correcting it brings the patient just that much nearer to chronic nephritis, cardiovascular changes, cerebral apoplexy or some other grave condition that represents the pathological fulfilment of a deranged metabolism, the inevitable result of wrong living. Physicians have been quick to recognize the necessity of correcting high blood pressure and much has been done in bringing the patient's mode of life into something like compatibility with the demands of physiology. The quantity and quality of food are regulated, the excretory organs are looked after, exercise and general hygiene have their due share of attention, and yet one most important factor in the treatment is generally overlooked—the correction of the functional derangement of the organs of internal secretion and digestion involved in the pathologic process. All other rectifying influences may amount to little if the glands of internal secretion and digestion are not restored to something like normal functional integrity.

Intestinal Putrefaction: The great majority of cases are toxemic in origin and by far the largest number come from intestinal putrefaction due to the excessive ingestion of food—particularly animal protein—or a functional incapacity of the digestive glands to deal with the quantity and quality of food ingested. Just how the toxins from intestinal putrefaction cause a rise in blood pressure is as yet not definitely determined but it is thought they cause hypersecretion of certain glands of internal secretion, particularly the adrenals.

Von Noorden says: "Adrenalin and the entire chromaffin system appear to play a part in the regulation of the blood pressure. Hypertrophy of the chromaffin system is a frequent finding."

Sajous says: "All these main causes of arteriosclerosis when reduced to their simplest expression, can thus be summarized by this one word; intoxication.

"What is the relationship between this general toxemia and the adrenals? Suggestive in this connection is the fact that all but one of the morbid conditions (the exception being alcohol, which has not been studied in this connection) known to provoke arteriosclerosis have also been found to cause over-activity of the adrenals."

In these cases it is assumed that toxins elaborated in the intestine stimulate the cells of the adrenal medulla to hypersecretion. On the other hand, it is now known that the products of protein putrefaction in the bowel are closely allied in their chemical make-up to adrenalin and that their presence in undue amount in the blood stream would occasion a rise in the blood pressure similar to that produced by injections of adrenalin itself. Probably the toxins act in both ways in producing abnormal tension.

Starling, in his "Human Physiology," says: "Schäfer and Oliver found that a watery extract or decoction of the suprarenal bodies, when injected into the circulation, caused a very great rise of blood pressure, brought about chiefly by constriction of all the blood vessels of the body. The active substance responsible for this rise was found to be limited entirely to the medulla, infusions of the cortex being without influence on the blood pressure. . . . Owing to the rapid destruction of adrenalin, relatively enormous doses have to be given by mouth in order to produce any effect on the blood pressure. There is, however, a whole series of substances more or less allied to adrenalin in chemical constitution which undergo less rapid destruction and can therefore be administered as drugs in the usual way. Dale and Barger have recently described three such substances as occurring in infusions of putrid meat and as forming the most important of the active principles of ergot. . . . Such substances may be formed in minute quantities during the normal processes of putrefaction which occur in the alimentary canal."

The Adrenals and the Pancreas: There is, therefore, good evidence for assuming that the rise of blood pressure is due either to an overproduction of adrenalin or to the excessive production in the intestine of bodies chemically akin to it. But we must not rest with the assumption that the malefic process stops there. That is simply one stage in the establishment of the vicious cycle. It has long been known that there is a physiologic antagonism between the adrenals and the pancreas but it was hitherto thought that the antagonism was confined to the medullary portion of the adrenals and the pancreatic tissue producing the internal secretion. It is now known that hyperactivity of the adrenals has also an inhibitory influence on the external secretion of the pancreas—that secretion which is by far the most important one in digestion.

Sweet and Pemberton (*Arch. Int. Med.*, Sept. 15, 1912) report that injections of adrenalin, given when the pancreatic flow is greatest, inhibit it, and, if the dose is large enough, will stop pancreatic secretion. After the blood pressure returns to normal indicating the passage of adrenalin from the system, the pancreatic flow returns. The flow may be varied at will by regulation of the dose of adrenal extract. Removal of the suprarenal glands causes a much increased flow of pancreatic juice. They conclude: "Since removing the adrenals induces a flow and since injections of epinephrin then inhibit the flow; and since the flow returns when the effect of the injection wears off (which last can be repeatedly demonstrated in one animal), it is difficult to escape the thought that there is normally some such relation between these glands."

Duodenal Insufficiency: It will be seen from this that any treatment of high blood pressure which excludes specific attention to pancreatic insufficiency and adrenal hyperactivity is necessarily incomplete. Pancreatic insufficiency is due either to exhaustion of the cells of the gland itself or to exhaustion of the mechanism that produces the hormone secretin, which initiates and maintains normal pancreatic activity. This hormone is evolved in the epithelial wall of the duodenum. Not only does it maintain the normal digestive function of the pancreas, it excites the flow of bile and the intestinal juices as well. Secretin thus correlates the activities and maintains the normal physiological balance of the pancreas, liver and small intestine, and when the activating influence of the bile and the enterokinase of the succus entericus on the pancreatic secretion is considered, one can readily comprehend the far-reaching effects of morbid processes in the duodenum—that portion of the gut which, in abnormal conditions, is the spawning ground for the vast majority of the disorders of metabolism.

The Thyroid and Gonads: Among the other glands that show depreciation in the majority of cases of hypertension are the thyroid and the gonads. T. Bodley Scott has pointed out that in women it is especially about the menopause that we find the minor symptoms of hypothyroidism and at the same time we also find the early symptoms of arteriosclerosis and high blood pressure. He thinks that as a rule hypothyroidism is associated with hypertension and that this increasing tension is what one would naturally expect from deficiency of thyroid secretion. He also believes that the connection between hypothyroidism and arteriosclerosis is a very close one, and that the early treatment of the first will often prevent the development of the latter. It is relevant to point out that the symptom of hypertension usually begins to show itself at the time that the sexual powers are waning, denoting perhaps that there is some interwoven relationship between the thyroid, the gonads and arterial tension. If this be so it naturally follows that the physician is making no mistake in employing gland extracts which will awaken and reinforce the functions both of the thyroid and the sexual glands.

One notably benign feature concerning the use of organotherapeutic extracts in the treatment of high blood pressure is that there is practically no danger of an undue lowering of the tension such as might happen with the use of ordinary drugs. Recognizing that a new physiologic limit begins with hypertension it is needless to demonstrate that the blood pressure cannot be reduced below that limit with safety. This danger might much more easily arise from the indiscriminate use of drugs than from properly selected doses of suitable organotherapeutic extracts. Using these extracts in the treatment of high blood pressure the arterial tension should never be in danger of being reduced below the new physiologic limit of safety.

NOTE.—For particulars of the various organotherapeutic measures that should be adopted in the treatment of high blood pressure see the last four pages of this issue.

General Pershing's Message through the New York Bible Society

To the American Soldier:

Aroused against a nation waging war in violation of all Christian principles, our people are fighting in the cause of liberty.

Hardship will be your lot, but trust in God will give you comfort; temptation will befall you, but the teachings of our Saviour will give you strength.

Let your valor as a soldier and your conduct as a man be an inspiration to your comrades and an honor to your country.

Pershing
Aug. 10. '17 Comdg.

Contemporary Comment

BLOOD PRESSURE IN THE AGED*

The trouble with generalities is that they are too general. Thus the saying that a man is as old as his arteries, while it bears a certain amount of truth, must not be accepted too unreservedly. Nevertheless, the question of blood-pressure becomes a more and more important one as the span of life draws near the allotted three score and ten, and this should not be estimated by a casual feeling of the pulse on one side, a glance at tortuous temporals, or the patient's account of vertigo, headache, etc. The most accurate methods available must be used and their results interpreted by the most modern knowledge of the subject.

In this connection two recent articles by Dr. L. M. Bowes (*Journal of Laboratory and Clinical Medicine*, Jan. and June, 1917), may be quoted. He studied three hundred and eleven cases, all but two of the patients being between sixty-five and ninety-five years of age. In the first of the two articles, Bowes calls attention first to the technique and the necessity for taking readings of both sides, as they usually vary considerably, especially in arteriosclerosis, although it must be borne in mind that the pressure may be low in this condition, if chronic myocarditis is supervening. Bowes further concludes that high systolic pressure associated with high diastolic pressure, indicates cerebral hemorrhage or nephritis; a sustained hypertension, both of systolic and diastolic pressure, indicates cerebral hemorrhage, while hypotension means cerebral embolism; a sustained high systolic with a low diastolic is suspicious of cardiac trouble, especially aortic regurgitation; a high pulse pressure is frequent in arteriosclerosis and aortic regurgitation and a sustained high pulse pressure usually results in a failing heart; a systolic pressure of one hundred may not keep a man from his daily business; lowering blood pressure means failing heart, and acute enteritis lowers blood pressure.

In his second paper the author gives the results of his studies of diastolic pressure. When this was high (above 95) he usually found some abnormal condition,—cerebral hemorrhage, mental symptoms, valvular heart disease, or the like. The diastolic pressure may be raised or not in arteriosclerosis, depending on the heart and kidneys.

**Medical Record*, Sept. 8, 1917.

He found it low in aortic regurgitation and chronic myocarditis. Bowes studied fifty patients who had been hard smokers for from forty to seventy years, but was not able to determine that this habit had the effect on the blood-pressure which is popularly supposed. He found some old men who had been inveterate smokers all of their lives who had a systolic pressure of from one hundred and sixty to one hundred and ninety mm. and diastolic pressures of from eighty to ninety. The writer lays especial stress on the diastolic index which he says may prove of great value—in surgery, for example, just before the amputation of a limb.

These studies remind us that, in spite of a wealth of casual allusion to the subject, too little use is made of the sphygmomanometer in daily practice. A careful examination of both the systolic and diastolic pressures of both sides of the body and interpretation of these results in the light of such work as this of Dr. Bowes, may aid greatly in diagnosis and prognosis. One fact in its favor is that it is not too difficult a diagnostic method for every-day use.

A CONCEPTION OF NEURASTHENIA.*

The term neurasthenia is employed to cover so wide a field that not a few physicians are even yet sceptical regarding its existence as a morbid entity. Specialists have ascribed its causation to those affections in which they are chiefly interested. . . . Leonard Williams in the *Practitioner* for July, 1917, joins the chorus and gives his views with regard to its causation. As befits one, who is peculiarly sensitive to the wiles of the endocrine glands, he declares his belief that when these glands become inactive, the subjective symptoms of neurasthenia become vocative and even vociferous. Moreover, he holds that neurasthenia being a circulatory matter, should not provide cases for the neurologist but rather for the cardiologist or surgeon. As for treatment, the remedy lies in the purification and the correct composition of the blood supply. The purification refers to drainage and the good composition to the tribute of the endocrine glands. In short, Williams insists upon the practical identity of the symptomology of true neurasthenia with that of suprarenal insufficiency.

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*Medical Record, August 4, 1917

Articles of Interest

CLINICAL NOTES ON SUPRARENAL INSUFFICIENCY.*

By Dr. L. Babonneix,

Physician to the Paris Hospitals.

Some twenty years ago a patient was admitted to the Saint-Antoine Hospital, under the care of Professor Gaucher, for ordinary acute tonsillitis. In three days his appetite had returned, he was able to sleep, his throat had cleared up and he was about to be discharged when he was suddenly seized with vomiting and abdominal pain, the temperature fell, the extremities became cyanosed and the pulse miserable. It was not long before he had an attack of faintness during which he died. Post mortem the suprarenals were found to be completely destroyed in contrast with the integrity of the semilunar ganglia.

The case seems at first sight to be devoid of any particular significance yet it proved pregnant with consequences inasmuch as it was the starting point of important researches at the hands of Prof. E. Sergent. It enabled him, in association with Dr. Leon Bernard, to establish that certain acute syndromes of toxic aspect were due solely to sudden arrest of the suprarenal functions, to define the part played in pathological processes by these glands, which had so far only been of interest to physiologists, and ultimately to form an ingenious theory of which none at the present time can afford to be ignorant.

This hypothesis assumes that the suprarenals, being indispensable to life, (Brown-Sequard, Abelous and Langlois) their secretion cannot become deficient without producing serious disturbances which, in the aggregate, constitute suprarenal insufficiency.

Nothing is easier to understand than these disturbances if we bear in mind that the adrenals discharge two essential functions, viz., angiotonic and antitoxic, that the latter neutralizes the toxic principles introduced to, or formed within, the economy thanks to the lecithine produced by the cortical layer, and that the former maintains the blood pressure at a certain level by means of adrenaline, a product of the medullary substance. It follows that any diminution of secretion must determine two sets of symptoms, viz.: The accumulation of undestroyed toxins accounts for digestive disturbances; anorexia, vomiting, colic, constipation and diarrhea, and nervous symptoms such as asthenia. The sudden fall of blood pressure has for result certain disturbances of the circulation; dilatation of the ventricles, acceleration, weakening and irregularity of the heart beat, smallness of pulse, pallor, the white line and tendency to faintness. Should the diminution of secretion go as far as total suppression, the asthenia merges into paralysis, the blood pressure falls still more and the accidents gradually get worse until the final syncope. Whichever happens we are in the presence of suprarenal insufficiency, acute or chronic, total or partial, hereditary or acquired; "it stands in the same relationship to the adrenals that thyroid insufficiency does to the thyroids and hepatic insufficiency to the liver. It dominates their pathology being common to all their destructive legions of which it is the almost inevitable sequel."

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*_Le Monde Médical_, July, 1917. Translation _Med. Fortnightly and Laboratory News._

Having thus defined suprarenal insufficiency it remains for us to pass its principal manifestations in review:

It has long been known that in certain acute infections circulatory troubles occupy a foremost place, in fact they govern the course of the disease giving rise to the adage. Pulsus cito et mire vacillans angustiæ summæ cita mors, wrote Huxham. His successors described the "weak heart of fever." Graves noted that in subjects suffering from malignant scarlet fever the pulse tends to fail so that bleeding was contra-indicated. Nearer to our own times Dr. Bernheim describes a cardiac form of typhoid fever in which attacks of cardiac failure come on early and death soon, almost inevitably, supervenes. Sevestre refers to the cardio-gastric syndrome of diphtheria of which the fundamental elements are cardio-vascular asthenia and vomiting which invariably culminate in syncope.

These phenomena which, on the strength of text-books, we have attributed to the most various causes: bulbar intoxication, organic or functional lesions, disturbances of the myocardium, neuritis of the vagus, etc., are in reality dependent simply and purely on suprarenal insufficiency. But how does it come to pass? There are three possible ways. Sometimes, as in this case, the gland is the seat of old-standing lesions and there remain only a few shreds of parenchyma to carry on its function. Once these shreds are destroyed the secretion falls to zero. In other instances, by reason of a sort of congenital debility, the

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gland is only just able to suffice for the ordinary requirements of the organism. Should these be increased, should the quantity of toxins thrown into the blood stream necessitate immediate neutralization, the task is beyond it, it becomes exhausted and dies in harness. In a third category of cases an infection causes acute massive lesions therein amounting to total suppression.

This same conception enables us to solve a number of problems relating to chronic infections. Why in tuberculosis subjects is the weakness so excessive, the blood pressure so low and the decalcification so rapid? Simply because their sclerosed or caseous suprarenal glands no longer secrete sufficient adrenaline and this substance, in addition to its vaso-motor action helps in large measure to fix lime in the tissues. Why does Addison's disease seem to be made up of two distinct diseases? Simply because the lesions are double involving both the suprarenals and the semilunar ganglion. To the former are due the asthenia and the circulatory disturbances, to the latter the melanodermia. When these are lacking then the symptoms are wanting. In this way we get a syndrome of pure, chronic, capsular insufficiency, the significance whereof escaped the older observers who, for want of anything better, classed these cases as incomplete Addison's disease.

Down to the last few years neurology made one think of the old maps of Africa in the center of which ancient geographers inscribed, as the spirit moved them, terra incognita or hic sunt leones. This was the time when neurasthenia was ascribed to a constitutional state, fits to a tendency to convulsions, and tetany to the contracture diathesis. We have changed all that. Thanks to Dr. Sergent we have learned to recognize suprarenal encephalitis and to familiarize ourselves with its multiple aspects. Acute, it is apoplectic, comatose, delirious or meningitic. Chronic it is characterized by neurasthenic manifestations. While he was at it this enabled him to assign its proper place in nosology to chorea. For a long time neurologists classified this as a neurosis, but we are no longer in the humor to listen to this tale. It is essentially an organic disease. Everything goes to prove this, everything including the circumstance that it is sometimes complicated by curious motor disturbances, less paralytic than asthenic, which yield in a few days to the administration of adrenaline.

Suprarenal insufficiency is likewise to be credited with the disturbances that follow anti-typhoid vaccination or injections of salvarsan and, more particularly, to chloroform anesthesia. It, too, is to be incriminated when we are called upon to solve one of the most exciting problems of forensic medicine viz. sudden death. How does this occur and what causes it? Observers have long allowed their imagination to run riot on this subject. Some ascribed it to rupture of an aneurism, others to atheroma of the coronaries, and each observer bolstered up his thesis with statistics. But all in vain! When closely scrutinized the statistics show that in the immense majority of instances there is neither aortitis nor coronaritis. As a rule in subjects who die suddenly the suprarenals are found to have undergone profound changes to the exclusion of any other organ. So much so that in future no case of the kind should be accepted unless the state of these glands is specifically noted.

But let us drop forensic medicine and pass on to surgery. We all know that patients after certain operations, remain, as it were, collapsed and this state of shock but too often culminates fatally. Or, in spite of the fact that the operation has passed off without any accident, they succumb to syncope a few days later unless indeed we witness the supervention of acute dilatation of the stomach with incessant vomiting. Previously to Dr. Sergent's researches such cases were put down to shock due to irritation of the peritoneum and the gastric dilatation to inhibition. With regard to sudden postoperative death, surgeons were pleased to have it attributed to a medical cause viz. embolism. The worst of it is that shock occurs only after abdominal operations, that inhibition is only an idle word and that embolism occurs mostly in text books. Is it not vastly more satisfactory here again to invoke suprarenal insufficiency, infectious or toxic, supervening suddenly when, the last shreds of gland being destroyed, the secretion ceases?

In obstetrics again special attention has always been directed to the so-called incoercible vomiting. After attributing this to hepatic insufficiency most authorities now ascribe it to villotoxemia incriminating the ovum with its active syncytial cells and its young villi which are so abundant early in gestation. In other words it is to the fetal organism that we must look for an explanation of the maternal intoxication. But how can villotoxemia set going the vomiting? Evidently by virtue of concomitant adrenal insufficiency as is shown by the excellent results of organotherapy and even more so by the existence in most cases of the kind of elements that constitute the adrenal syndrome.

According to the manner in which these elements are grouped the affection runs its course more or less rapidly. This syndrome may simulate quite a number of affections: upset stomach, appendicitis, cholera, peritonitis, intestinal obstruction and poisoning. In the subjects of grave traumatisms it may lead us to suspect fracture of the skull. It is obvious therefore that its diagnosis is a matter of the greatest importance. Nor is it less indispensable to prognosis. If the white line—a conclusive sign of insufficiency—be well marked, the blood pressure low, with well-marked tendency to attacks of faintness, we must, without losing a minute, start the suprarenal treatment. With this object in view we may employ either extracts of the gland or adrenaline for both curative and prophylactic purposes. The treatment is indicated in all acute infections especially the eruptive fevers, diphtheria and typhoid fever, most chronic infections, especially pulmonary tuberculosis in which it advantageously completes the recalcifying treatment introduced by Dr. Ferrier, in most forms of intoxication, and in various surgical and obstetrical affections. Its results are constant, immediate and often astonishing.

Such, briefly set forth, is the theory promulgated by Dr. Sergent. It had to run the gauntlet of severe criticism at first. It was reproached on the one hand with upsetting the established order of things, and, on the other, with an inadequate experimental basis. Everyone thought they were doing it honor by attacking it. The theory has triumphed over one and the other and has now become classic, it has been crowned with success and this on its own merits. It was original, it consisted in developing one of the new ideas of which Claude Bernard has left us an immortal definition. As distant from teutonic pedantism as it is from Byzantine subtleties it goes straight to the mark along a road bathed in light. Clinical in its origin, scientific in its methods, it betrays in its minutest details the hand of an attentive, sagacious observer. It offers a doctrinal interest of the highest order. Lastly, and especially, it enables therapeutics to take a step forward. It has enabled us to snatch innumerable existences from the brink of the grave and if really medicine is the art of curing disease adrenal insufficiency is more than the work of a master, it is a great medical discovery.

PREVENTION AND TREATMENT OF ARTERIOSCLEROSIS.*

"There exist two chief agencies for the production of arteriosclerosis: 1. A hyperactivity of the adrenals, causing a rise in blood pressure. 2. A degeneration of the thyroid gland, which, when normal, antagonizes the first by lowering the blood pressure. Although from the above mentioned facts high blood pressure cannot be considered as the chief cause of arteriosclerosis, still no doubt it certainly contributes to it; for each time there is a rise in the blood pressure more blood is forced through the arteries, thereby causing them to dilate; and after a repeated number of such dilatations the elasticity of the vessels will eventually be impaired, especially so in the aged, where one part of the elastic fibers is already replaced by connective tissue. As a result of the arteriosclerosis the passage of blood through the capillaries will be impeded, and in consequence the work of the heart will be increased; likewise the nutrition of the walls of the vessels will be diminished. The best preventatives of arteriosclerosis will therefore be: 1. To avoid all agencies which may tend to cause excessive activity of the adrenals; and 2. To increase the activity of the thyroid.

"Moderation in food is necessary above all things, for much food causes an increase in the abdominal circulation and a larger amount of blood to be carried through the vessels; if the food consists of much meat, then its viscosity is augmented, as previously stated, which indicates that a vegetable diet, with milk, and little or no meat, is the best but too large quantities of milk should not be taken at one time.

"Much bodily and other exercises, in excess, such as too much climbing, should be avoided, as they promote arteriosclerosis by frequent excitation of the splanchnics and adrenals. As Romberg observed, there is sclerosis of the arteries in the extremities of persons who do much physical labor, and Remlinger found the same in the lower extremities of peasant women who walked a great deal.

"Not only by diet, chiefly vegetarian, is the viscosity of the blood diminished and the circulation facilitated as found by Determann, but also by means of iodine administered in the shape of iodide of potassium or iodide of sodium. . . . Besides inorganic iodine, it would appear to us logical to try organic iodine preparations, such as thyroid extracts, the principal element of which is iodine. For the above reasons it is also necessary to take special care of the condition of the kidneys, which can be done, as we have shown, by hygienic and dietetic measures already described in the special chapters of this work. An improvement in the condition of the kidneys, and probably also in the arteriosclerosis, may, in our judgment, be obtained by the administration of kidney extracts, with which we will deal more fully in the chapter on the treatment of old age by organic extracts.

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*Lorand "Old Age Deferred."

"According to Edgreen, about 25 per cent. of the cases of arteriosclerosis is caused by alcohol. It acts by causing a constriction of the small vessels (Traube), just as does adrenalin.

"But much more harmful in the production of arteriosclerosis is tobacco. According to Claude Bernard, Huchard, Basch, Oser, Isaac Adler and Hensel, tobacco produces a constriction of the small blood-vessels. Thus nicotin, adrenalin and alcohol have similar actions, which also corresponds to the observations of Sir Lauder Brunton. We have had a great many smokers among our arteriosclerotic patients; but, on the other hand, we quote further on the cases of some great smokers who lived to a very old age as we have seen. But this latter class is not numerous.

"Similarly, the hygiene of the intestines is of the utmost importance, especially as poisons generated in the intestines play a leading part in causing arteriosclerosis, according to Huchard, Senator, and others. We must take great care to have a daily evacuation of the bowels, and especially to prevent flatulence, for this distention of the colon or the stomach, by carrying the diaphragm upward, may interfere with the expansion of the lungs and thus produce a mechanical hindrance to the movements of the heart and a free circulation of the blood. Those with a tendency to angina pectoris must specially avoid such dangerous courses. Hill climbing, during which not infrequently such people suffer sudden death, should also be avoided. More than from 1 to 1½ liters of liquids per day should not be allowed."

* * *

Etiology of Diabetes.—In a preliminary statement to a discussion of his treatment of diabetes by a modified starvation plan, (Safian, *New York Medical Journal*, August 25, 1917), points out that diabetes is essentially a disease of hyperacidity and occurs most frequently in

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persons who consume large quantities of proteins and fats. These persons are subject to acid intoxication as evidenced by one group the members of which are subject to gout. In others the pancreas suffers as the result of the unequal strain put upon it, and undergoes certain degenerative changes resultant in a diminution of its internal secretion.

It appears that a degree of acidosis exists even before the appearance of glycosuria due to faulty metabolism. This acidosis may not be sufficient to give urinary symptoms but a hypoalkalinity of the blood does exist and this mild acidosis produces the degenerative changes in the Islands of Langerhans. Safian says that the usual habit of placing all the blame on the carbohydrates is not justified. It is just as important to control the protein and fat metabolism as that of the carbohydrates in the diabetic patient.

* * *

"**Minor Maladies**" by Leonard Williams is a book of especial interest to the general practitioner. Dr. Williams is not only a writer with rare command of the English language but is also an original thinker, especially in the practical application of opotherapy. The following is from preface to 4th Edition: "It is an easy thing to prescribe a drug, but it is not an easy thing to readjust your outlook. The man who discovers a new drug—like Maclagan and his salicylates—is acclaimed as a deliverer; the man who preaches a new gospel, as Lister, Arbuthnot Lane, or George Gould, is despised by his contemporaries and stoned by his elders. . . Sir James Mackenzie is fond of insisting that our present methods of investigation are not sufficiently directed towards the discovery of disease in its earlier stages, that we are content impotently to contemplate the full-blown, whereas we ought to search for buds and tendencies. In this criticism I see much justice, and I believe that the serious study of what are called minor maladies will in this way lead to the prevention or forestalling of many serious diseases. Still more earnestly do I believe that the study of the whole field of the Internal Secretions will enable us to detect and correct morbid tendencies with a degree of success which has been denied to the older methods. The microbe—the seed—has ruled the immediate past; the future is with the soil, the endocrine glands."—(Balliere, Tindall & Cox, London. Pub.—Wm. Wood & Co., New York.)

Brief Abstracts

Lime Therapy in Tuberculosis.—The editor of *The Medical Council* writing on the administration of calcium salts in tuberculosis says that the value of these has been greatly overrated. When used he prefers calcium lactate or calcium citrate. However, he says that it must be conceded that none of these agents entirely supplies calcium deficiency since comparatively little of the calcium is absorbed and assimilated and it is quite probable that food rich in calcium may supply the lime salts that are lacking quite as adequately as will calcium in the form of a drug. However, he fails to point out another factor in calcium nutrition and that is, that no matter how lime is given, whether as a food or a medicament, meagre results are bound to follow unless the calcium absorbing and fixing powers of the organism are at a normal standard. Recent investigations have shown that the suprarenal glands play a great part in calcium metabolism, and that hypoadrenalism goes hand in hand with calcium starvation.

* * *

Treatment of High Blood Pressure.—In hypertensive conditions, H. B. Hemenway, (*Medical Council*, November, 1917), recommends citric acid or the citrates for the reduction of the viscosity of the blood. He says that chloride of sodium and other chlorides increase viscosity. Water must be freely taken into the system. It not only cleanses but it supplies the needed fluid for the blood. Physical or mental exertion must be restricted in proportion to the increase of blood pressure. Either tends to increase the heart action. On the other hand, except with very high blood pressure, some exercise seems beneficial.

* * *

Frequency of Tuberculous Lesions at Autopsy.—Reinhart (*Correspondenz-Blatt für Schweizer Aerzte*), made a special study of 460 cadavers at the Pathological Institute in Berne, seeking for evidence of tuberculous lesions. Twenty-eight new-born infants were free from all traces of the disease. Of seventy-two other children, all under sixteen, only twenty-one showed evidence of infection. Of another sixty children only twelve had died of tuberculosis. In adult bodies tuberculosis lesions were found in 96.38 per cent. out of a total of 360 subjects. There were only thirteen negative cases in the series and these were found in younger adults. The tuberculosis mortality was highest between thirty and forty, rapidly declining after the latter age. While the figures given confirm the wide prevalence of tuberculosis they also show that in most people it heals, and accordingly the Reinhart study should beget optimism, as the disease takes a relatively small toll of life among those affected.

* * *

The Edema Symptom in Starvation Treatment of Diabetes.—Edema, or its concomitant phenomenon, gain of weight, despite complete withdrawal of food and reduction of liquids, Croftan (*Journ. A. M. A.*, November, 1917), says is a starvation phenomenon indicating forced catabolism of body tissues beyond the limits of safety; a degree of tissue destruction that constitutes the main element of danger in the severe types of diabetes, that rarely occurs spontaneously in the milder types of the disorder, and that a rational therapeutist should attempt by all means to prevent and to counteract.

Croftan considers that the "pancreatic rest" demanded by Allen is certainly not favored under these conditions; that nothing presumably imposes a greater strain on the hypothetic internal function of the pancreas than the disassimilation of products derived from forced tissue catabolism.

Edema occurring in starvation cures is a sign, therefore, to resume feeding; it is a danger signal that, if neglected, and especially if associated with nausea, severe headache and tremors, in Croftan's experience, invariably either leads to most alarming coma or, if this is prevented by large doses of sodium bicarbonate, leaves the patient, as far as his tolerance is concerned, in much worse condition than before the starvation plan was inaugurated.

Edema during "starvation" can be prevented by the administration of pancreatized oatmeal-alcohol-glycerin clysmata; Croftan has found that they do not interfere with the rapid sugar reduction, that they prevent the enormous formation of acetone bodies and materially contribute to the comfort of the patient.

Treatment of Backward Children.—Treatment, according to McCready (*Medical Record*, December 15, 1917), may be divided into prophylactic, hygienic, medical and educational. The prophylactic measures should date not only from earliest moment of conception but should be applied to the parents at an even earlier period. Ante-natal hygiene is of an importance not generally realized yet, though upon it depends, to a large extent, the future stability of the race. An important phase of the prophylaxis of hypoplasia during the gestational period is the treatment by glandular substances of ductless glandular insufficiencies of a minor character in the mother. In the immediate treatment of hypoplastic children the therapeutic implication is pluriglandular. He has found pluriglandular therapy of great value as an aid to the stimulation of metabolic processes and the forces of growth by bringing into equilibrium the various glands with their common though tangled relationships, with resulting improvement in nerve tone in the mentality and body resistance.

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Glandular Therapy.—At a discussion of diseases of the ductless glands at the New York Academy of Medicine (*New York Medical Journal*, September 1st, 1917), Dr. Robert T. Frank said, in regard to corpus luteum and ovarian therapy, to which beneficial effects had been ascribed, it could be stated that corpus luteum had a specific biological effect limited to the uterus and breasts. He had never been able to find any action which promised to benefit the nervous symptoms at the time of the menopause. If an active preparation were given it should relieve functional amenorrhea if exhibited for a long time; but no menstruation would occur while corpus luteum was given. Menstruation would not occur until the drug was withdrawn. It would help local conditions in infantilism but in vasomotor troubles no effect could be anticipated as far as any experiments up to the present time had shown.

Dr. D. M. Kaplan stated that in treating patients with extracts of various glands, it was not safe to give pure extract because of its uncertainty; in his opinion it was best to give the entire gland substance in as native a state as possible. No one could tell how many more substances were present in the adrenals that were of as great importance as adrenalin; or in thyroid as thyroidin, or in pituitary as pituitrin.

In referring to thyroid therapy Dr. M. Allen Starr said that certain mental conditions could be produced experimentally by the administration of glandular extracts. Many cases of depression and melancholy had been benefited by thyroid gland preparations which counteracted the effect produced by the toxic agent in the blood. There was a field for the investigation of mental defects associated with glandular inactivity.

As to thyroid therapy, Dr. N. W. Janney was of the opinion that it might be conservatively stated that far too large doses of the preparation of this gland were usually prescribed; the therapeutic feature of active thyroid preparations was optimal when the doses were quite small.

* * *

Mammary Extract in the Treatment of Uterine Fibromyomata.—After giving a record of his individual experience with mammary therapy in the treatment of uterine fibroids, W. A. Briggs (*California State Journal of Medicine,* September, 1917), says that it indicates the remarkable, but perhaps not invariable, influence of mammary extract on uterine fibroids and menorrhagia, their most frequent and distressing symptom. Mammary extract, even with prolonged use did not seem to produce any untoward results. In some of the cases he combined it with hydrastis and ergot and occasionally though rarely the combination produced more or less gastric disturbances, which subsided, however, on the suspension of these two drugs. Other untoward results, either from the combination or from the mammary extract alone, Briggs had not observed even after prolonged use. On the contrary there was generally a distinct improvement in the physical health as well as in the morale of the patients, probably chiefly attributable to the arrest of the menorrhagia, the relief of pressure symptoms, and the relief of mental strain due to fear of operation.

The mammary hormone probably antagonizes the follicular hormone or inhibits its production and thus moderates or prevents an excessive menstrual molimen and its consequent hyperemia, menorrhagia and local nutritive disturbances. The effective dosage therefore would seem to depend on the degree of excessive ovarian activity—the greater this functional activity the larger the quantity of mammary extract required to inhibit or antagonize it. A daily quantity of the extract representing from twenty to fifty grains of the fresh gland was used in the cases here reported. The dosage in several of the cases was too small. This accounts perhaps for the comparative or even absolute failure of the treatment in a few of the cases and possibly also for the absence of gastric irritation occasionally noted by others. At present Briggs says he usually prescribes thirty to forty grains daily and, in refractory cases, increases to fifty or sixty.

Pregnancy seems to be the only positive contra-indication to the use of mammary extract. In two of the cases reported, however, its continued use did not prevent pregnancy. In both of these cases mammary extract was given for some time before and for three months after conception and in a third case (in consultation) for the last four months of pregnancy without provoking interruption.

* * *

Pituitary Disease.—After a study of one hundred selected cases of pituitary disease, Abrahamson and Climenko, (*Journ. A. M. A.*, July 28, 1917), present the following conclusions:

The posterior and middle lobes of the pituitary gland secrete a substance or substances which have, according to our observations, the following among other properties:

1. It does not influence sugar metabolism (sugar tolerance is not a sign characteristic of pituitary disease).
2. It controls the salt content on which the electrical conductivity of the blood depends.
3. This control is not exercised through the nervous system.
4. Disease of the posterior and intermediate portion of the pituitary gland disturbs the fixed ratio of the salt content of the blood which the secretion or secretions of that gland normally maintain.
5. Slight disturbance in the control induces alteration in the salt content of the blood and leads to polyuria, if there is renal sufficiency, or to a water logging of the tissues, if there is renal insufficiency.

* * *

Retention of Ovarian Tissue After Hysterectomy.—At a meeting of the American Gynecological Society, Dr. William P. Graves (*N. Y. Med. Journ.*, Aug. 11, 1917) drew the following conclusions: Specific

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surgical menopause symptoms consisted chiefly of vasomotor disturbances in the form of hot flushes. Theoretically, vasomotor changes of the artificial menopause were due to a break in the uteroovarian functional harmony, by which the physiological balance of the glands of internal secretion was upset with consequent dysfunctional activity. After extirpation of the uterus, vasomotor disturbance ensued with approximately equal frequency whether the ovaries were retained in situ, totally ablated, or transplanted. Retention of ovarian tissue after hysterectomy was of little or no physiological value and might be productive of serious harm to the patient.

* * *

Thyroid Gland in Relation to Gynecology and Obstetrics.—Dr. David Marine, (*N. Y. Med. Journ.*, Aug. 11, 1917) said that it might be stated that there was evidence in man of a thyroid sex gland interrelation recognizable in the female in association with the development of secondary sexual characters, with the menstruation, and with pregnancy and also in the male at puberty, but to a very slight degree. The meager evidence available would tend to indicate that the interstitial cells of the ovary and perhaps, also, the adrenal cortex played a major rôle in this relation in the female, as certainly the cells of Leydig did in the male. The thyroid enlargement was of the nature of a work hypertrophy to stimulate metabolism identical in appearance and so far as they knew, different only in degree from that seen in simple goitre. Both of these reactions could be controlled and prevented either indirectly by giving iodine or directly by giving the iodine containing hormone in physiological doses.

* * *

Relation of the Parathyroids to the Female Genital Apparatus.—Dr. Eugene H. Pool, (American Gynecological Society, *N. Y. Med. Journ.*, Aug. 11, 1917), summarized his observations as follows: No direct relationship had been established between the parathyroids and the female sex organs, and no morphological changes in the parathyroids had been noted during pregnancy, yet apparently there was a connection between the parathyroids and the sex processes in the female. Tetany, the clinical evidence of insufficient parathyroid function, was somewhat prone to occur in menstruating, pregnant, and puerperal women, as well as in patients suffering from gynecological diseases or who had undergone gynecological operations. The cause of maternal tetany was now referred to parathyroid insufficiency. The function of the parathyroids was apparently closely connected with calcium. There was reason to believe that maternal tetany and lactation tetany were associated with calcium deficiency. Latent tetany, or a subtetanic condition, was much more common in pregnant and puerperal women than was usually assumed. Tetany in newborn infants the offspring of tetanic mothers, was usually fatal within a short time after birth. In the treatment of maternal tetany, the administration of calcium in large doses was followed by beneficial results in the great majority of the cases.

* * *

The Placenta as a Gland of Internal Secretion.—At a meeting of the American Gynecological Society (*N. Y. Med. Journ.*, Aug. 11, 1917), Dr. Robert T. Frank, of New York, said that the experimental work of the last decade proved that Halban was correct in ascribing to the placenta an action upon the uterus and breasts. Placental extracts, mainly the lipoid fraction, rapidly induced hyperplasia of the uterus and breast, gland tissue and nipples in castrated or in non-castrated animals. The chemical substance which induced these changes was thermostabile, very resistant to strong alkalies and acids, and completely soluble in ninety-five per cent. alcohol. The substance appeared identical in its physical, chemical and biological properties with a similar substance obtained from the corpus luteum. The substance could exert its influence in the absence of the thyroids, adrenals, pancreas, or in the absence of thyroids and adrenals combined. In view of the apparent identity of corpus luteum and placental substance, the question arose whether the placenta acted merely as a storage reservoir for corpus luteum secretion during the latter half of pregnancy or whether the placenta elaborated a hormone of its own.

* * *

Ovarian Therapy in Kraurosis Vulvae.—Speaking before the American Gynecological Society (*N. Y. Med. Journ.*, Aug. 11, 1917), Dr. George Gellhorn, of St. Louis, said he had observed great improvement in two cases of kraurosis vulvæ. In one there had been permanent relief after feeding the patient ovarian extract; another patient was temporarily improved after injecting the extract. Neither suggestion nor deception was permitted to enter. The sole criterion was a change from the dry glistening unyielding tissue to a soft, moist, and pinkish mucosa which bore no evidence of scratching. A temporary restoration of locomotion in two cases of senile osteomalacia with the same therapy was hard to explain on the ground of suggestion.

* * *

Ovarian Organotherapy.—After extensive experience with various ovarian extracts, Graves (*Journ. A. M. A.*, Sept. 1st, 1917), gives the following conclusions:

1. Studies in ovarian organotherapy are at present necessarily confined for the most part to clinical observations. Such observations, though admittedly inaccurate, may, to a limited extent, be of scientific and practical value.
2. Personal clinical experience with preparations of ovarian substance has revealed that preparations of the corpus luteum alone are less efficacious therapeutically than are those of the whole ovary.
3. Theoretical knowledge and scientific experimentation tend to show that an important part of the ovarian internal secretion is elaborated by the interstitial cells.
4. It is probable that the interstitial cells correspond to the lutein cells of the theca interna of the atretic follicle. In some animals these cells become disaggregated and appear as glandlike masses (interstitial gland); in others they remain confined to the follicle by the outside envelope (theca externa).
5. The interstitial cells, therefore, correspond to the theca lutein cells of the corpus luteum.
6. The interstitial cells of the ovary are analogous to the testicular interstitial cells of Leydig, which are known to elaborate an internal secretion.
7. Ovarian therapy, for its best effectiveness, should include at least the product of the interstitial cells. Preparations should, therefore, comprise the ovarian stroma, in order to take advantage of the atretic follicles.

8. Preparations made from the corpora lutea of pregnancy proved too toxic for practical use.

9. Preparations made from the ovaries of pregnant animals, with exclusion of the corpora lutea, proved superior therapeutically to preparations of whole ovaries of nonpregnant animals that included the corpus luteum.

10. The superiority of the follicular products of pregnancy is explained by the fact that during pregnancy, follicle atresia is especially marked, and is accompanied by a corresponding increase in the activity of the interstitial cells.

* * *

Thyroid Dosage.—The dose of thyroid extract is quoted in most text-books at 3 to 10 grains; three times daily; a dose so large that it would be ludicrous were it not so dangerous. The proper dose is from one-tenth grain to 1 grain, three times daily; the more a patient requires the drug, the smaller is the initial dose which he will tolerate.

If it is intended to give thyroid extract over a period of several weeks, it is necessary to make observations upon the temperature and pulse-rate. If the drug is really required, the temperature is almost without exception subnormal, especially in the evening, and the pulse rate is as a rule slow. When the temperature rises to normal, the drug should be suspended, at any rate for a time, and the pulse-rate, whatever its initial figure, should never be allowed to go above 95 without calling a halt. . . A sudden and profuse nasal catarrh sometimes surprises people who are taking thyroid extract, and unless the physician realizes that such a thing is possible, he may attribute the catarrh to some ordinary cause and fail to discontinue the drug.

We know that metabolism is under the direct control of the internal secretory glands. We know that these glands preside over growth and development in infancy and childhood, that they are essential to mental, physical, and reproductive efficiency in adult life, and that they are responsible for the maintenance of katabolic balance in the period of decline. It is therefore no exaggeration to define the constitution of an individual as the resultant of his internal secretions. (*Minor Maladies*—Leonard Williams).

THE RATIONAL TREATMENT OF HIGH BLOOD PRESSURE.

Organotherapy is a potent weapon in combating high blood pressure and preventing the dire sequelæ of which it may be the forerunner. Here one is copying Nature's methods and employing her own weapons instead of depending for the most part upon drugs which are often toxic substances foreign to the organism.

In high blood pressure we have usually the following conditions to deal with:

1st. Duodenal, hepatic and pancreatic insufficiency.

2nd. Undue intestinal putrefaction with a consequent hyperadrenalism.

3rd. Thyroid and gonad insufficiency.

The therapy employed comprises:

1st. Use of an extract of the duodenal mucosa to improve function in the duodenum and thereby stimulate the pancreas, liver and duodenal glands to increased activity. Improved duodenal function means an increased production of secretin. Secretin is the natural stimulus to the production and outpouring of the digestive secretions of the pancreas, liver and intestines. This can be done by the use of Secretogen Tablets.

2nd. Administration of Trypsogen to depress adrenal hyperfunction.

3rd. The immediate correction of the dysfunction of the glands of internal secretion more immediately concerned in arterial hypertension.

The exhibition of Secretogen by giving 2 or 3 Secretogen tablets, before meals, is a logical and desirable means of establishing and maintaining normal liver, duodenal and pancreatic function. Secretogen stimulates the production of the pancreatic ferments, thus tending to overcome intestinal putrefaction; excites the increased production of secretin and enterokinase, and so stimulates the liver cells that the normal antiseptic bile flowing freely as a result of the secretion stimulus, will not only inhibit and prevent abnormal conditions in the biliary passage but will provide Nature's own antiseptic for the intestinal tract.

The question of depressing adrenal hyperactivity now arises. Secretogen, by ensuring more thorough digestion, relieving constipation and lessening intestinal putrefaction, will do this to a large extent, but it will be wise to supplement its use by the exhibition of Trypsogen as well. Trypsogen contains the homostimulative principles and the ferments of the pancreas (trypsin predominating) and the bromides of gold and arsenic. The pancreatic ferments will assist in inhibiting intestinal putrefaction, especially of proteid, thus further diminishing the supply of the toxins which act as a whip to the adrenals, while the bromides of gold and arsenic will directly depress adrenal activity. It is also assumed that a preparation of pancreas containing its homostimulative principles will assist in reducing adrenal hyperfunction.

A curious but benign effect is often noted in the treatment of high blood pressure cases with Secretogen and Trypsogen. After two or three days the patient may complain that he has a certain feeling of lassitude and drowsiness, and that his former high pitch of activity is lowered. The activity was essentially morbid and the feeling of lassitude or drowsiness is radically benign. Either Secretogen or Trypsogen, by reason of the effect they have in inhibiting putrefactive processes in the intestine, deprive the adrenals of the spur which is continually goading them to hyperactivity. Such a patient is high strung and ever "on edge." When the organism under the influence of Secretogen and Trypsogen has adapted itself to the new and benign order of things the problem of lassitude will solve itself. Further, it will be found on inquiry that the patient who has been taking Secretogen and Trypsogen has a far less voracious appetite than formerly and particularly so for food of animal origin. In this connection, L. F. Bishop, whose insistence on the importance of the study of cellular physiology rather than organic morphology in the treatment of cardiovascular disease has gained him great attention, says: "You—any of you—could give up meat and not miss it, but if you were poisoned by it you would miss and crave it. It requires a good deal of strength of mind for a person with advanced arteriosclerosis to give up offending proteins."

The importance of this cannot be overestimated. It is a point that has never received the consideration it deserves. The truth is that a meat-eater who is consuming his favorite pabulum in excess of his capacity to deal satisfactorily with it is in much the same category, as far as stimulants are concerned, as a chronic alcoholic. He is accustomed to his stimulant and his body cells crave it. When his stimulant (in this case the toxins elaborated by putrefaction) is cut off he suffers from the reaction, just as the whiskey addict does.

Secretogen and Trypsogen, therefore, not only strike at the cause of the morbid process which gives rise to high blood pressure, they help to combat an effect of wrong living that has to be overcome if the patient is to tread the narrow pathway that leads to recovery.

Dosage of Secretogen and Trypsogen in high blood pressure: Two tablets of Secretogen before meals and three or four Trypsogen Tablets after eating. After two or three weeks the Trypsogen may be omitted and Secretogen alone given.

IMPORTANT: *In cases complicated by albuminuria prescribe Trypsogen without gold and arsenic.*

The following points are of prime importance in the treatment of high blood pressure: (1) Less stimulating diet, omitting spices, etc.; (2) Diminished meat; (3) Increased vegetable diet; (4) Diminution of fluid; (5) Less salt; (6) Limitation or discontinuance of alcoholic beverages and tobacco; (7) Warm baths; (8) Systematic exercise.

ANTIPUTREFACTIVE DIET: Cornwall relies chiefly on milk, bread and cereals for protein, and secures extra calories from butter, olive oil, fat bacon, the starch of the roots and other vegetables, the sugar of fruits and honey, and milk sugar. One quart of milk, 12 ounces of cooked cereal, and six slices of bread will give about 55 grammes of protein and 1300 calories. The vegetables, fruit, butter, bacon, etc., given to bring the calories up to between 2000 and 2500, will add enough protein to make the total of that food element about 65 grammes. If more protein is required he increases the milk or cereals, or adds cheese, or allows a small quantity of animal protein; in many cases of putrefaction toxemia a small portion of meat, fish, poultry or eggs can safely be allowed once to four times a week; and if such a relaxation of the diet increases the protein too much, the milk, cereal or bread can be diminished to make the protein ration balance. Vegetables and fruits, though poor in protein content and of small fuel value, have an important place in an antiputrefactive diet because they supply necessary salts, add variety to the diet, which is often monotonous to the patient, relieve constipation, and are "filling."

To restore the abnormal internal secretion condition met with in high blood pressure, it is advisable to use

HORMOTONE WITHOUT POST-PITUITARY.

In this connection the following letter from the English clinician, Dr. T. Bodley Scott, is of decided interest:

> "You were so good as to put on the market some time ago, partly I believe in consequence of an article of mine in "*The Practitioner,*" a new Hormotone Tablet which contained no Post-Pituitary. This I have found very valuable, as one can give it freely in elderly people whose blood pressure is above normal. I have found that your Hormotone Without Post-Pituitary not only does not raise pressure, but that it has a decided effect in lowering it. In nearly all my cases in which a gradual reduction of pressure is wanted, I think it is one of the most valuable remedies we have. The nitrites, of course, produce the more immediate effect, but one not nearly so lasting. Hormotone Without Post-Pituitary causes no gastric disturbance like the iodides, and no headache like the nitrites."

In "*The Practitioner*" for November, 1917, Dr. Scott again refers to the value of Hormotone Without Post-Pituitary. He cites an astonishing case in which "the patient apparently being *in extremis,*" Hormotone Without Post-Pituitary had a surprisingly good effect.

Dose of Hormotone Without Post-Pituitary for adults is 1 or 2 tablets 3 times daily before meals.

Secretogen, Trypsogen and Hormotone Without Post-Pituitary are for sale by chemists and druggists generally and prepared only by

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The Metabolist

A RECORD OF PROGRESS IN THE STUDY OF THE
INTERNAL SECRETIONS AND METABOLISM

VOL. III 1918 NO. 4

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The Metabolist

VOLUME THREE 1918 NUMBER FOUR

Editorial

"SPANISH INFLUENZA" AND INTERNAL SECRETIONS.

That the processes by which toxic substances in the blood are counteracted and rendered harmless are closely related to the mechanism of internal secretion is now generally believed. It naturally follows that susceptibility to infections is largely due to diminished efficiency of these glands in their protective role. Their connection with infections is clearly demonstrated in the great susceptibility shown in subjects of hypothyroidia and hypoadrenia to such a disorder as tuberculosis or the marked tendency shown by such subjects to cardiac failure in pneumonia, diphtheria and other infectious diseases.

We are beginning to have better ideas of the autoprotective resources of the body. Strange as it may seem the old humoral origin of disease held by the ancients is finding justification in the light of biochemical research, particularly that part of it dealing with internal secretions. The correlation of function of the organs of the body is due to the glands furnishing these secretions. Hence their use in practical medicine is theoretically sound and practically expedient. Both thyroid and pituitary extracts have been used with good effects in strengthening the defensive resources of the body.

Sajous says that pituitary extract is useful in infectious disorders because it enhances the immunizing activity of the blood and the tone of the cardiovascular system. Renon and Delille found that pituitary extract favorably influenced the course of influenza, rapid recovery resulting in patients as old as 63 and 80 years. These results were confirmed by Azam in *the infectious form of influenza.* He found that the cases which showed an intense and prolonged asthenia were favorably influenced and the convalescence hastened.

Greater stress is now laid on the participation of more than one internal secretion in the development of a morbid process, and this is equally true when treating of any grave condition met with in the course of an infectious disease. Pituitary extract may be of value in grippe (due doubtless to the adrenal principle it contains) but it is altogether unlikely that this gland is the only member of the endocrine system functioning below normal. The thyroid with its well-known antitoxic and protective role is undoubtedly a partner in the morbid process. In any event the stimulating effects of small doses of thyroid on the adrenals is well known and, further, it has been observed that the combination of thyroid and pituitary is frequently of much greater service than the use of either medicament alone. Treating of the role of the thyroid in immunity, the *Journal A. M. A.*, (Nov. 13, 1915) says: "In view of the part played by the thyroid in maintaining the health of the body it would not be surprising if disturbances of the function of this gland should be found to favor the development of the infection, if not by direct interference with the formation of antibodies, then in some more or less indirect manner, such as disturbances of the functions of the leucocytes."

Extracts of the thyroid, pituitary and gonads combined* have shown their efficacy in the treatment of grippe, especially in hastening convalescence, and it is probable that if susceptible individuals were to undergo such medication during the time of an epidemic that it would tend in great measure to ward off attack or to lessen its severity if it should develop.

We cannot put it better than by quoting Sajous again when he says "through a study of the ductless glands we may, perhaps, eventually learn to develop the main object which therapeutics should fulfil—that of directing and controlling the defensive resources of the body."

The term "grippe" or "influenza" has been used clinically in a very inexact way and certain local epidemics have been definitely proved to have been non-specific while others have included varying proportions of true influenza and miscellaneous infections of the upper-respiratory tract.

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*See ad. p. VI.

The present epidemic has, in the main, so far as reports are at present available, been one of genuine influenza though, of course, this does not imply that every catarrhal case occurring in the same period, has been of this nature. The question arises whether the term "Spanish" has any real significance, or whether Spain, having been relatively free from influenza for a considerable time, afforded especially susceptible human material when a source of infection was accidentally introduced. Certain European observers have claimed to have discovered a specific germ differing from the true influenza bacillus. In view of the remarkable facility with which germs have been discovered (?) by various observers for all sorts of clinical infections and the contradictory testimony of more careful and less biased observers, these claims should be accepted with reserve. At any rate, it is to be regretted that the term "Spanish Influenza" has been used so widely by various American authorities, in the absence of a demonstration of a new bacterium and especially so when we consider the popular alarm that the adjective has caused.

Another highly important point is whether the pneumonic complication, noted in a fairly large minority of cases, is exceptional and whether the pneumonic lesion is due to an independent infection or is part of the reaction of the influenza bacillus itself. This is by no means an academic problem as it has an important bearing on the use of immunizing measures.

Without in the least intending to pronounce an unfavorable verdict, we may say that we have seen a good many cases develop after the administration of vaccine, some of them of considerable severity, after its use as a prophylactic measure or as a method of abortive treatment. Thus, without attempting a statistical argument, we feel convinced that vaccine in its present state and as administered is by no means a success either as a prophylactic or therapeutic measure.

The debilitating effect of influenza has, perhaps not been so thoroughly appreciated as it should be. Experience in military camps has led to a true appreciation of this factor, especially with regard to the predisposition to tuberculosis. It is, however, doubtful whether this predisposition is in any sense specific or any greater than can be explained by general depression plus vulnerability of the respiratory tract.

That the conception of a true neurasthenia as an adrenal insufficiency is coming to be widely accepted may be noted from recent articles on the subject. Tom A. Williams, Campbell Smith, Leonard Williams and other writers have insisted on the recognition of the adrenal origin of neurasthenia. T. A. Williams insists that many patients who show symptoms of neurasthenia with low blood pressure, loss of mental elasticity, fear that their work shows depreciation and that they are afraid of making wrong decisions and who show a vacillating and indecisive frame of mind, are many times suffering from adrenal insufficiency. It is doubtless true that many of the symptoms of neurasthenia conform to the description of hypoadrenia given by Sajous. However, a pluriglandular disturbance is nearly always in evidence, although, of course, its symptoms do not stand out so clearly. Naamé, in his endocrinological studies, attributes the neurasthenic syndrome to pluriglandular hypofunction. Naamé's observations have the weight of personal experience because he claims to have been virtually regenerated by pluriglandular treatment.

Turning to another form—sometimes termed "high grade neurasthenia"—one generally finds a blood pressure above normal. These cases are chiefly among subjects above the age of 40 and occur in both sexes. In women they are generally seen about the time of the menopause and in men between the ages of 40 and 50. Indeed such a condition has been described as "change of life" in men. DeFleury has seen in 201 cases such a form of neurasthenia in which the nervous and mental symptoms had followed signs of sluggish nutrition and autointoxication. Treatment in many of these cases had proved unavailing as attention had been directed solely to the mental symptoms and the physical basis for the disorder had been overlooked. In these cases the psychic condition is distinctly subordinate to the somatic and they are usually amenable to medical measures. DeFleury attributes this form of neurasthenia to thyroid insufficiency and his observations have been confirmed by those of T. Bodley Scott. But we think it will be found that this thyroid insufficiency also leads to gonad hypofunction and the reaction resulting from this may amount to no small share in developing the psychic picture of such cases. The treatment here consists in promoting and maintaining a sanitary condition of the intestinal tract which is best accomplished by the use of duodenal extract,

combined with pancreas if necessary and the exhibition of extracts of the thyroid and gonads to restore the glandular hypofunction.*

A CORRECTION.

Our attention has been directed to an error in a souvenir booklet published by us entitled "The Doctor's There, A Note of Appreciation." The title "The Doctor's There" is also that of a poem which we first saw in the publication of the Annual Oration delivered before the North Carolina State Medical Society, Morehead City, N. C., by Dr. L. B. McBrayer of Asheville, N. C. This appeared in the *Charlotte Medical Journal* for June 12, 1907. It was used as a quotation but we erroneously assumed that it was written by Dr. McBrayer himself and so gave him credit for it. We have recently been advised by Dr. W. A. MacKenzie of Fruitland Park, Fla., that he is the author of the poem and that he wrote it as an appreciation of Dr. W. G. Moore of St. Louis, Mo., who was his ideal as a physician. This poem, Dr. MacKenzie says, was written by him in 1903 and published in the *Medical Mirror* and afterwards republished in several languages. The sentiment is so appropriate and so beautifully expressed that we took it as the key-note and the most appropriate title for our collection of tributes of appreciation to the physician. We are extremely sorry for our error and gladly take this opportunity of correcting our mistake. If any physician reading this does not recall having received a copy of "The Doctor's There" we shall be very glad to send him one on application.

Thyroid Therapy: In general the principle could be established that a therapeutic effect, aside from the questionable thyroid treatment of obesity, was accompanied by an increase in the amount of nitrogen retained. Conversely, the administration of too large quantities of thyroid preparations caused a reduction in the nitrogen balance even when no other signs of toxicity were present. It might be conservatively stated that far too large doses of the preparations of this endocrine gland were usually prescribed; the therapeutic effect of active thyroid preparations was optimal when the doses were quite small.—(N. W. Janney, M. D., *N. Y. Med. Jour.*, Sept. 1, 1917.

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*See ad. outside back cover.

Contemporary Comment.

CARBOHYDRATES IN DIABETES.*

In the progress of our knowledge of the nature of diabetes there has been a marked reaction against the entire withdrawal of the carbohydrates from the dietary of the diabetic. For a time there was even a tendency to administer carbohydrates as a curative measure, and the "carbohydrate cure" seemed all but established. Then came the understanding that the carbohydrates cannot be withdrawn from the dietary of the individual without increasing the tendency to acidosis, or of precipitating a grave acidosis where previous to the carbohydrate withdrawal there was only a mild one. It is found that when the carbohydrate withdrawal is persisted in, acetone bodies soon appear in the urine. As the sugar disappears the acidosis appears. It must be understood that the presence of sugar in the urine is of importance only as indicating that the sugar is not being oxidized or utilized. As long as enough sugar is oxidized there is no harm in some or even a great deal passing through unoxidized, but as soon as the amount oxidized becomes deficient then acetone appears. Even in rather severe diabetes the organism can oxidize some sugar. If in these cases not enough carbohydrates are given to satisfy the meager demands and oxidizing powers of the organism, acidosis follows, so that in cases treated with carbohydrate withdrawal, in whom acidosis threatens, carbohydrates must be administered to forestall the event. Moreover, with the withdrawal of the carbohydrates, so necessary for the production of heat and energy, the organism draws upon the proteins of the body for its carbohydrates. It is shown, in fact, that with the increase of the carbohydrate intake there is a decrease in the protein consumption. Whether the protein of the body is utilized in great quantities, or more proteins are consumed to make up for the carbohydrate deficiency, increased protein metabolism means a large increase in the metabolic burden of the body. For the organism with a defective metabolic system, as evidenced by the presence of diabetes, this added metabolic activity is very harmful. Besides, protein metabolism is the most potent factor in the production of acid; indeed, protein food may be called acid food. In addition to the natural hypoalkalinity of diabetes there is, then, the increased acid production—and acidosis is bound to follow. The administration of carbohydrates reduces the protein metabolism sufficiently to prevent acidosis, where the carbohydrate oxidizing power is not too far gone.

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*Boston Medical and Surgical Journal, June 6, 1918.

When the value of administering carbohydrates in diabetes was first understood it was thought that certain carbohydrates behaved differently from others. Oatmeal was supposed to have a special value as a carbohydrate cure because it was thought that the starch in it had a special action; that it had certain special ferments or extractives of value; or that it reduced the permeability of the kidneys to sugar. None of these hypotheses has any substantiation, and any value that oatmeal has in the so-called "oatmeal cure" must be ascribed to the general value of carbohydrate administration, where there is a defective carbohydrate oxidation, and where the organism is using up its own body proteins to make up the deficiency naturally withdrawn because of the metabolic condition, or artificially withdrawn in a mistaken notion of treatment.

The most recent conception of the proper treatment of diabetes takes into consideration the metabolic disturbance at the base of the disease, as well as the part that the carbohydrates play in the disease. The starvation treatment has for its object, therefore, the resting of the metabolic system for the period of the starvation. The subsequent dietary treatment no longer contemplates the withdrawal of the carbohydrates, but rather that they be given in sufficient quantities for the needs of the system, without necessitating drawing on the body proteins. On the other hand, it is not intended to tax the metabolic processes by administering large quantities of food. Every element of food is reduced to the minimum needs of the body. When it is remembered that a reduction of half of every one's dietary would be beneficial rather than harmful, there need be no fear of underfeeding in an organism whose metabolic system is damaged. Most of all, is the protein kept at a minimum in order to reduce the tendency to acid production.

THE PROTEINS IN THE CAUSATION OF DIABETES.*

Whatever the dietetic errors that provoke the diabetic condition it now seems certain that it is not the carbohydrate alone that is at fault. Primarily diabetes occurs only in an individual whose metabolic organ-

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**New York Medical Journal*, July 27, 1918.

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ization is very weak, but it will not occur unless provoked by some gross and persistent dietetic abuse. Perhaps overeating is the most potent factor in its causation. On the other hand, in races that consume large quantities of farinaceous food with only a minimum of proteins or fats, diabetes is very rare. Neither underfeeding nor poverty is a cause; it is rather a disease of the rich.

When the expensive proteins are consumed in large quantities by those who can afford them and by those who lead a sedentary life, diabetes is likely to follow. It is more than likely that even without a proper balancing of the food, a reduction in the total quantity of food consumed would in itself reduce the incidence of diabetes. It is the protein element that must be curbed rather than the carbohydrates in diabetes. In the newer understanding of this disease this is realized, and far from withdrawing the carbohydrates they are often advocated as a cure for diabetes. It is from this that the so-called oatmeal cure received its reputation. Heretofore the dietetic treatment of diabetes contemplated an almost unlimited supply of proteins and a complete withdrawal of the carbohydrates. Yet it was understood that the threatening of an acid condition was a sign for the restoration of the carbohydrates, in spite of the increase of the sugar output.

Overindulgence is perhaps the most important factor in the production of a systemic hypoalkalinity. The taking of food in which the proteins predominate increases the acid production and increases the hypoalkalinity. The proteins, in fact, are acid foods. It is pernicious in any glycosuria to allow an excessive meat diet. Very often a marked limitation or even abstinence for a period will of itself cause the disappearance of the sugar. Moreover, the defective utilization of the sugar is not nearly as ominous to the organism as an increase in the acid state of the body as a result of protein intoxication or excess. Indeed, it is because of the defective utilization, where only a small amount of sugars can be oxidized at one time out of the amount supplied, that the sugars must be pressed so that at least this small amount can always be carved out of the total supply. There is no harm in the presence of sugar in the urine. It is merely an index of the condition. The amount of sugar only shows how much of it the system could not utilize.

Before much improvement in the carbohydrate utilization can occur the nitrogenous equilibrium must be established. The prescribing of a meat diet in this weakened metabolic organization but increases the nitrogenous inequilibrium. Those individuals who exist on the diet heretofore prescribed for the diabetic—that is, high protein and low carbohydrate—are the ones most likely to be attacked with diabetes. Diabetics get along much better on a normal well balanced diet than on any special diabetic dietary that has not the balancing as its chief purpose. Because the basic cause of diabetes is a weak metabolic organization the diet must be at a minimum in order to tax the metabolic process least, but the diet must favor the carbohydrates rather than the proteins. The diet is the provoking element in a damaged organization. With normal metabolism no one can foretell how much abuse the organism can stand without injury. If organotherapy has any value in the treatment of diabetes it is because the basic metabolic weakness in diabetes is probably of glandular origin. It is most probable that not only the pancreas but also the other glands of internal secretion are concerned, and the gland extracts usually administered supply a deficiency that the defective glands cannot.

Tom A. Williams (*American Medicine*, Aug. 1917) says: "Various authors have given the following as some of the symptoms of neurasthenia: failing strength, prostration after exertion, cold extremities, anemia, constipation, loss of control of attention, weakness of memory, weak will power, inability to perform mental work, incapacity of decision, abdominal throbbing from pulsating aorta.

Compare the now well-known symptoms of hypoadrenia: asthenia, sensitiveness to cold and cold extremities, hypotension, weak cardiac action and pulse, anorexia, anemia, slow metabolism, constipation and sometimes psychasthenia, as well as others which appeared in the cases reported herewith.

Hypoadrenia may result from the wasting of old age, the toxins of the infectious diseases, hemorrhages into the substance of the gland due to high blood-pressure, or perhaps from exhaustion by long-standing emotions. So that neurasthenia, we may realize, is hypoadrenia. We know something of its pathology, but no one ever knew of a satisfactory pathology of neurasthenia. The symptoms of hypoadrenia stand out clearly which never could be said of neurasthenia; and armed with this more definite knowledge, we can formulate and carry out better ideas for its treatment. . . ."

Articles of Interest

THE REAL NEURASTHENIA.*

BY LEONARD WILLIAMS, M. D.

Physician to the French Hospital.

. . . The *neurasthenia* of Weir-Mitchell which was treated—and still is—by stuffing, slapping, and seclusion, is now recognized as a complex symptom which may be due to many causes.

The Arbuthnot Lanes would have us believe that it is manufactured in the intestines, by kinks, bands, and adhesions; that its cure by the classical methods is due to the recumbent posture, the kneading, and the slapping; and that, in a really scientific scheme, the stuffing would be replaced by purging and the seclusion by a ceinture. The Ernest Clarkes impose upon us as a therapeutic faith more important than a Christian belief, that slight errors of refraction, when uncorrected, tap the central nervous system as a lancet taps a vein. The St. Clair Thomsons point to the deficient oxygenation of the blood which follows in the wake of obstructed upper air passages, and hold the deviated septum to be the villain of the drama. There are some obscure and stupid people, of whom I am one, who are so sensitive to the wiles of the endocrinic glands that these glands constantly appear in their writings in unexpected and irrelevant connections. According to these people, when, for any reason, the glands become inactive, the subjective symptoms of neurasthenia become vocative and even vociferous. Then there are those who purvey pyorrhœa as a first cause; and again, those who find diagnostic perfection in a pile. On the somersaults, tergiversations, and other acrobatic feats alleged in this connection against so dignified an organ as the uterus, I forbear to enlarge further than by saying that the word "neurasthenia" seems as clever at producing a curette as a cat at producing kittens.

Now, all and more of such explanations of the symptom complex may be correct; which is the same thing as saying that there is no such thing as neurasthenia. This is a fact to which men are now awakening, and there is danger lest the swing should go too far. That is our stupid way in medicine; witness the acute disfavor into which venesection most undeservedly fell, and the acute favor in which bug-worship is at present rioting to the neglect of the normal defences and in defiance of common sense. For there is, after all, a real neurasthenia. Before the Greek terminologist came from America to cast his meretricious mantle over it, we called it shock. Where men live among grim realities, as our kinsmen live at the front, it is still called shock; for the term "Shell shock" covers a multitude of shocks other than those caused by explosives; some emotional, others grossly physical; all are traumatic. It is curious to note that, when life reverts to primitive conditions, language follows suit. In war time, the effeminate, pseudo-scientific "neurasthenia" is promptly superseded by the simple, direct, descriptive Anglo-Saxon "shock." That is a precious improvement which we should seek to perpetuate. Real neurasthenia is traumatic neurasthenia, and traumatic neurasthenia is shock. The others—the intestinal, the ocular, the nasal, and the endocrinic, except in so far as they are begotten of shock—are not true neurasthenias; they are plausible impostors, now in process of being unmasked.

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* *The Practitioner*, July, 1917.

But "shock" itself stands in need of definition. Shock does curious and unaccountable things. Why it should produce death is easy to understand, and will presently be explained; but why it should produce some other things is difficult of comprehension. It will produce chorea, Graves' disease, and other dramatic phenomena. With regard to chorea, we have it on the authority of Sir Dyce Duckworth that this malady is essentially "rheumatism of the brain"—a profound and illuminating pronouncement—which stands as the most remarkable contribution to scientific medicine which this dispensation has produced. Graves' disease has been described as a chronic condition of fright, fight, and flight—a good enough description, if you will look beyond the bulging eyes and tremulous hands, to visualize the overactive suprarenals, behaving chronically to produce the disease, as they behave suddenly in the presence of these emotions. Shock is an arterial matter and the suprarenals hold intimate converse with the arteries.

I have said that the real neurasthenia or shock is a circulatory matter. That is true. If I had said, as I almost did, that it was not a neurological matter, it would have been very nearly true, though not quite. It is a matter which has so far been entrusted mainly to neurologists. That is a mistake. If any kind of specialist is fit to hold a monopoly on the subject, then he should be a cardiologist or, even more fittingly, a surgeon. The spotlessly over-alled craftsman who goes down to the peritoneum in rubber gloves, knows a great deal about shock; it might even with justice be said that men like Crile, Lane, and Lockhart-Mummery have instructed us to far better purpose than any neurologist who was ever born. The neurologist's interest in the matter is centered in the medulla oblongata. When this is granted, we may dismiss him; for the subsequent phenomena of shock are well within the competence of the physician or general practitioner to understand or expound.

The proper circulation of the blood is second in importance only to its proper composition. Its composition is determined by the efficiency partly of the excretory organs and partly of the ductless glands. Its circulation is maintained by the central nervous system; partly by the medulla and partly by the local centres of the cord. When one set of vessels dilates, like the gastric for the purpose of digestion, another set must contract; otherwise, the general pressure would fall, to the detriment of the whole circulation, and hence of special and vital areas. There is thus continually in operation a see-saw of local contraction and dilatation to supply our every day's most common needs. These local changes in arterial calibre are under the control of the local centres; and the finesse of their play, could we but witness it, would surely seem finer and more delicate than the subtlety of the most beautifully balanced mechanical device. In comparison, the part of the medulla in control of the circulation seems clumsy and heavy-handed, for the medulla has no local control. Its powers are confined to general orders. It can command a general dilatation, but it may not ordain a contraction here, to compensate a dilatation there. Nevertheless, the medulla is the very knot of life itself. As Clifford Albutt says in an inspired passage, "It knows no pause, no quiescence; let its vigilance be at fault for a few seconds, and the busy frame it governs will drop into silence." And the drop into silence is brought about by a drop in the calibre of the blood vessels, a drop so great that the circulation is not maintained, and the medulla, which has other vitalities among its dependents is itself starved of the essential sanguineous fluid. Verily, the fleetest and vilest of all vicious circuits. . . .

But the medulla not only initiates, it transmits. It originates and controls vitalities, but it also transmits potentialities. Within its narrow borders it encompasses all the activities, efferent and afferent, which make life worth living. It is at once the Clapham Junction, the Privy

Council, the See of Canterbury, and the M. C. C. of the central nervous system. So that though it may be wanting in finesse the medulla is pregnant with consequence. When you hit it hard enough in the face, you kill. When your blow is slightly less well directed, you stun; or in other words, the concussion produces effects which are bafflingly remote. With the immediate, we are not concerned, for they are not in dispute. It is round the remote that the terminological tangle rages. You have to consider not only the degree and accuracy of the blow, but the intimate texture of the material which receives it. A buck-nigger will accept with good temper, and even with obvious appreciation, a buffet which would lay President Wilson lifeless at your feet. You may do to the human carthorse that which you dare not do to the human thoroughbred. Then there is the same material to be considered in its relation to age. If subjected at 45 years to the collisions which at 15 he enjoyed in the football field, Jones's stomach would deliver up its immortal soul. There is, likewise, the question of sex. Assuming them to be of the same age, and drawn from the same class, you would not expect the nervous system of a Suffragette to remain unruffled by an explosion which you might be sure would leave Mr. John Burns as cool as a cucumber. The one would have hysterics at once, neurasthenia at length, and a rest-cure to finish; the other would proceed home, on foot, to read "As You Like It."

Now this drama of the medulla is in the main a circulatory tragedy. The quality of the blood is involved, but the chief mechanism is vasomotor. It is not safe to venture upon the part played herein by the ductless glands. . . . I shall confine myself to recalling a French saying, which is old, but in this connection, both interesting and pertinent. *"Se faire du mauvais sang"* means, literally, to make for oneself some bad blood. Metaphorically, it means to be irritated, agitated or worried. That worry and anxiety, especially when beginning suddenly, can actually cause a deterioration in the quality of the blood, to the extent of producing successive crops of boils in people who were previously in perfect health, is a matter which, to my mind, admits of no sort of doubt; any more than it is possible to deny that a sudden violent emotion may produce an attack of ordinary inflammatory big-toe gout. The glandular influence is sufficiently obvious in these phenomena, but I am concerned less with the mechanism than with the result. I desire to emphasize the fact that shock profoundly alters the composition of the circulating fluid, and that the malign influence may extend over a long period of time.

I have already said that in the matter of arterial calibre the medulla's power is confined to the general orders; that it can do no more than order a general contraction or a general dilatation. This is only another way of saying that what physiologists call the "tone" of the vessels, their maintenance in the state more or less midway between complete contraction and definite dilatation, is under the control of the bulb. When the bulb is in watchful health, this control is active and unerring. When it is out of health, things happen. One kind of toxemia may give rise to an undue pressor effect; another kind, to a depressor. These bio-chemical questions are functions of the endocrine system. In the case of trauma or shock, the effect is always depressor. If you hit the medulla in the face, or shake it, as a terrier shakes a rat, it falters. The contractile power is impaired, the vascular tone is lowered, the vessels dilate, the blood-pressure falls, the various organs are insufficiently supplied, and there emerges the *real neurasthenia;* a tremulous, elusive, emaciating phantom, full of subjectivities.

In the matter of one of the objectivities upon which it is open to us to inform ourselves, namely, the blood pressure, we have, unfortunately, become harnessed to mechanical appliances. It is not that I have aught to say against the use of the sphygmomanometer in its proper sphere—*bien au contraire*—but I am definitely of the opinion that its precision of record and its facility of manipulation have led some of us to credit this instrument with an informative power which it does not and cannot possess. The real neurasthenia is a case in point. What we want to know is not the record in mm. Hg. of the deliberate blood pressure in the recumbent posture, but the way in which that pressure behaves in changing conditions. A smitten medulla may retain enough of its pristine power to maintain a good pressure in a quiescent musculature, and yet be quite incapable of responding to a call, however slight, for increased pressure, where such is normally and physiologically necessary. It is not so much the actual blood pressure that we should seek to gauge, as the readiness of vascular response to the calls of daily life, postural, muscular, metabolic, and nervous. If we are to use an instrument at all, we must use it when the patient is recumbent, sitting, and standing, and compare the results. But there is a better way.

Leonard Hill says: "A useful clinical guide to the compensatory mechanism in man is afforded by the rate of the pulse on change of posture. If the heart becomes greatly accelerated on rising from the horizontal to the vertical position, the vaso-motor tone is deficient." Before this was written, the late Professor Huchard of Paris had studied this question, and was teaching that the normal difference between the upright and recumbent pulse-rates was from eight to ten beats per minute, and that a normal recumbent rate, which became "tachycardic" in the upright posture, indicated a serious want of tone in the peripheral arteries. In the true neurasthenia, a very wide divergence between the pulse-rates in these two positions is always present; and, what is worthy of note, is the fact that this is the only objective phenomenon which is present. The other so-called symptoms, such as tremors, ocular difficulties, abnormalities of gait and the like, are what neurologists distinguish as "functional," which is only a perverse way of designating a thing which is, in reality, within the control of the victim. The control has been lost; it is "held up," as the Americans say, in the medulla, which, being obliged to ration itself, confines its attention to vitalities, and allows such superfluous refinements as co-ordination to go by the board, until such time as it shall have sufficiently recovered to resume that sovereign sway, which it is the part of all well-bred medullas to exercise.

But our learned friend leading on the other side will promptly and very properly suggest to you that want of control by the higher centres is a characteristic of hysteria, and that the plaintiff lady who has been rattled in a railway accident, or buffeted by a bus, is, in reality, indulging in "the vapours" to display her sensibility. "Don't you think, doctor, that when this case is over, she will make very rapid progress to complete recovery?" Inasmuch as the symptoms of hysteria and the symptoms of true neurasthenia resemble each other so closely as to be practically identical so far as verbal description is concerned, this species of subtle thrust is difficult enough to parry, unless it is remembered that the difference in the two cases ante-dates the accident. In the case of neurasthenia, the control, once present, often conspicuously present, has been temporarily annihilated; in the case of hysteria, it has never been there to annihilate. The previous history of the plaintiff will bring this all-important distinction into pointed relief. A more difficult nut for the inexperienced to crack is the degenerate "soul" who, by claiming "the utmost for the highest," and snuffling about "the good, the beautiful and the true," has succeeded in convincing the unwary that she has always been possessed of complete control. In such cases, her husband, her female friends, and her other natural enemies should be carefully cross-examined.

In cases of true neurasthenia it is impossible to give a prognosis. Our learned friend's crafty suggestion that a verdict for substantial damages will hasten recovery is very much more correct than he knows. Such a verdict very materially contributes to the amelioration of the *mauvais sang* caused by the accident; the medulla is thus rehabilitated, the vascular equilibrium tends to become re-established, and progress becomes more rapid. As to treatment—how is one to treat a battered bulb except by the sedative of a purified and well composed blood supply? The purification refers to drainage, and the good composition to the tribute of the endocrine glands. Of the former, I will say nothing; it is so banal that few ever consider it. With regard to the latter, I permit myself to fling wide my restraint in a parting shot, and boldly call attention to the practical identity in the symptomatology of the real neurasthenia with that of suprarenal insufficiency.

The different periods of life could be said to be dominated by various glands. An old man had no use for the thymus, but he had use for adrenals; he was an adrenal individual. Constant secretion of the adrenals, however, produced in the adult conditions which were manifested by the blood vessels; this was due to the fact that he lived on the adrenals when the gonads no longer functioned. The baby lived on the thymus, the young man on the gonads, the old man on the adrenals. The thymus was the only gland in the body containing a trace of arsenic; witness the red cheeks of the young child. Constant changes took place in life coincident with the change from the thymus to the gonads and from the gonads to the adrenals. The first change was significant of puberty and all the stormy manifestations of adolescence; the second change, which might be designated the gonadopause, was equivalent to the cessation of function in the sex glands of man and woman.—David M. Kaplan, (*New York Medical Journal*, September 1, 1917).

Brief Abstracts

Antiscorbutics for Scurvy.—At a meeting of the Association of American Physicians, May 7, 1918, Dr. Alfred F. Hess of New York, emphasized the necessity of antiscorbutics in any diet. In ships, in the days of sailing vessels and prolonged voyages, there were always cases of scurvy. The civil population was also dependent upon antiscorbutics in the food, and it was not always realized how narrow the margin of safety was. In Ireland, when the potato crop failed, scurvy at once appeared. From the military point of view antiscorbutics were important. In Russia, during the war, there had been thousands of scurvy cases. In France, in one sector, of 1,000 men, 850 had the disease. If the war kept on this might assume serious aspects, and it was necessary to consider what foods were antiscorbutic. Experiments showed that dried vegetables soon lost antiscorbutic properties. Orange juice, if preserved, also lost this property. Orange peel, which was a waste product, seemed to have the property of preserving its antiscorbutic action. Its use in institutions where the price of oranges made their use prohibitive, would be an economic measure. It was found also that boiled orange juice, given in intravenous injection, acted like a charm in scurvy. Scurvy could be absolutely controlled by giving heated and neutralized orange juice intravenously, on a large scale.

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Thyroid Hormone in Relation to Metabolism.—At a meeting of the Association of American Physicians, May 7, 1918, Mr. E. C. Kendall reported that a definite chemical substance had been isolated from the thyroid gland, containing six per cent. of iodine. This was found to have a marked effect on cretinism and myxedema. The substance existed in two forms, an amino group and an acetyl one, which bore to each other the same relation as creatine did to creatinine. In the myxedematous patient the metabolism was forty per cent. below normal and could be increased to normal by the injection of this hormone. The iodine content of the hormone did not enter into its action, but merely increased the reaction of the functioning groups.

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Certain Phases of Hypertension.—At a meeting of the Association of American Physicians, May 7, 1918, Dr. E. S. Smith of Boston, said that to avoid brain disaster, hypertension must be controlled. Factors entering into normal circulation were the peripheral resistance of the vessels, the propulsion of the blood through the arteries, and the vasomotor control. Hypertension was often caused by accumulation of toxic end products of bacterial proteins. If it persisted it caused strain on the heart and cardiac fibres. The cases where arteriosclerosis had resulted from hypertension were different from the luetic type. In regard to treatment, attention was paid to focal infection, absolute rest was ordered, and the protein intake of the diet was limited. Digitalis was given, but no vasodilators, unless in extreme emergency.

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Fat Regulation in the Treatment of Diabetes Mellitus.—P. J. Cammidge (*British Medical Journal*, April 6, 1918) points out that in the treatment of diabetes mellitus control of the fat allowance is quite as important as regulation of the carbohydrate and protein intakes. Bloor was the first to carry out a systematic study of the fat content of the blood of diabetics. He found that out of thirty-eight cases a lipoid value of the blood in excess of the normal average was present in thirty-six, and in but three cases it exceeded the highest limit met with in healthy persons. A marked increase, up to 100 per cent. or more of normal values, was found in all severe cases, but as a rule the more severe and long standing the diabetic condition the more marked was the abnormality in the blood lipoids. The evidence at present available suggests that the excessive lipoid value of the blood originates in the fat of the food, and is due to the partial failure of the mechanism for dealing with fat arising from the essential nature of the diabetic state. Bloor found that there was no definite relation between high blood lipoids and the occurrence of acetone bodies in the urine. Moreover, that diabetic lipemia is not due to change in the reaction of the blood is indicated by the fact that the greatest possible reduction in its carbon dioxide capacity by acid poisoning produces no characteristic change in that direction. It would therefore seem that the tendency to imperfect utilization of fat in diabetes is not dependent upon any other feature of the disease, but is a primary phenomenon of the condition. Cammidge says that it may be taken as a general working rule that fat unbalanced by an adequate available supply of other food is poison to the diabetic, and that the craving of bread and other starchy foods is an expression of a natural want that should be dealt with by restoring the balance in the diet by reducing the fat rather than by increasing the carbohydrate, as is usually taught. He further points out that from experiments conducted by Allen, it seems reasonable to conclude that the hyperglycemia and glycosuria following excessive feeding with fat are due to a failure of metabolism consequent on the gain in weight above what the defective assimilative functions are able to cope with, and that any attempt to induce a high level of nutrition with fat results in an aggravation of the diabetic condition similar to that which follows a like attempt with carbohydrate or protein, although its effects are slower and more insidious. These observations make it clear that in addition to rendering the urine sugar-free by limiting the carbohydrate intake or adjusting the protein allowance, it is also necessary to ascertain the optimum amount of fat which will meet the needs of patients, prevent acidosis, and avoid the onset of glycosuria. Cammidge has obtained satisfactory results by the fasting treatment; in some cases in which sugar returned he found that an excess of protein was being taken and in others that the fat content of the diet was the difficulty, and when this was adjusted to the patient's metabolic powers the glycosuria promptly ceased and did not return. He states that in treatment the aim must be a steady weight which can be maintained without overtaxing the patient's defective metabolic powers. Gain in weight must be sacrificed to well-being and satisfaction of the appetite to length of days. Individualization of the diet, in which the allowance of carbohydrate, protein, and fat is regulated by the tolerance of the patient for each and by his powers of dealing with the diet as a whole, is the line along which the treatment of diabetes is developing.

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The Proteins as a Cause of Disease.—In an interesting article Dr. Robert C. Brown (*Medical Record,* July 27, 1918), emphasizes this new factor in the cause of disease and, treating of diabetes, says that it is freqently found in protein poison families and is often found in association with protein poison manifestations such as gout, eczema, migraine, hyperacidity, etc. This is a seeming paradox, but the inability to metabolize carbohydrates is not the cause of diabetes but the effect.

Diabetes is very rare in Japan and among vegetable eating people. It is found principally among meat eating people and is notoriously a disease of high living. He believes the cause of diabetes will be found to be in the damaging effect of protein on the pancreas and the ductless glands.

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Goiter in Pregnancy.—Dr. Leigh F. Watson (*Journ. A. M. A.*, September 14, 1918), sums up this question as follows:

1. Preexisting goiter, either simple or toxic in type, is usually aggravated by pregnancy.
2. It is believed that the symptoms and growth of hyperplastic goiter in pregnancy can usually be controlled by quinin and urea injections into a portion of the thyroid gland.
3. Should symptoms progress in spite of conservative measures, a rapid delivery is indicated. If the child is viable, cesarean section should be done.
4. Operation on the thyroid is indicated to relieve pressure symptoms of solid goiters. Cystic goiter may be promptly relieved by quinin and urea injections.
5. Pregnant women with subthyroid conditions should receive iodides or thyroid throughout gestation.

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The Acetonemic Syndrome in Children. — A. Rémond and R. Poux (*Bulletin de l'Académie de médicine,* May 28, 1918) deem cyclic vomiting only a single, separate manifestation of the acidosis of children. The cases of acidosis in which it is absent are more numerous than those in which it is present. The underlying condition is an essential functional disturbance of the liver, small intestine, and pancreas. Passage of the fecal matter from the small to the large bowel suddenly stops. The stools consist merely of epithelial debris and mucus, are colorless and practically odorless, vary greatly in frequency and amount, and may later become blood stained or of the green color of spinach. At once or within five or six hours, acetone or diacetic acid begins to appear in the urine, and in a day or two the breath is found to have an acid or stale odor. The temperature may be markedly subnormal or febrile, and often exhibits a paradoxical curve. A few of the cases encountered manifested nervous symptoms suggesting meningitis. Others simulated beginning typhoid fever or cholera infantum, while still others were first seen in a condition bordering on coma. The treatment applied consisted regularly of subcutaneous injections of a total extract of fresh pancreas and of sodium bicarbonate in large doses. In one particularly grave case a one per cent. alkaline solution was administered intravenously. In the remainder, from twenty to sixty grams of bicarbonate a day were given by mouth as well as by continuous rectal instillation. Temperature, nervous condition, stools, and urine returned to normal in a few days. Acetonemia through pancreatic insufficiency plays, as shown by cases previously wrongly diagnosed and treated unsuccessfully by other measures, a far more frequent role in children's diseases than has hitherto been thought. In all intestinal or nervous infections in children, an acetone diagnosis should be promptly made. The condition being recurrent, prophylactic measures should be instituted, such as elimination of cooked fatty articles from the diet, as well as of excess of meats, and the systematic ingestion of alkaline waters. The Vichy treatment seemed highly efficacious.

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The Pluriglandular Syndrome. — Leonard Williams ("MINOR MALADIES") says: "It is well for the reader to understand that the interdependence of the endocrine glands renders it very difficult in the present state of our knowledge to be sure which particular gland is at fault. It is exceedingly likely that some of what we now take to be manifestations of thyroid insufficiency of slight degree, are in reality due to insufficiency of some other gland, partly opponent and partly complemental, such as the pituitary or the adrenal, which may be stimulated into increased activity by the exhibition of thyroid extract. . . . In the case of adrenal insufficiency, some of them, notably the infantilism, the low temperature, the hairlessness and pigmentation are prominent symptoms. It is therefore evident that when one member of the endocrine hierarchy is at fault, the mere disturbance of the glandular balance is sufficient to produce certain symptoms of which one can only affirm that they point to a disturbance somewhere in the endocrine system—the pluriglandular syndrome, as it is called."

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Intestinal Antiseptics vs. Organotherapy.—(Leonard Williams "MINOR MALADIES"). In the objection which is sometimes urged against chemical intestinal disinfectants it must be admitted that there is much force. The objection points out that an efficient bactericide will kill not only the enemy microbes, but those friendly ones upon whose beneficent activities Metchnikoff insisted with such curious results. This is a very pertinent criticism, which it would be more easy than it is to dismiss as mere theory if the results of our present antiseptic therapy were always clinically satisfactory. In certain cases these chemical disinfectants succeed admirably, but in others they fail, and their failure reminds us that the real intestinal antiseptic is to be found in the intestine itself. If we could but evoke an increased activity of the natural defences, the necessity for such aids as thymol and benzonaphtol would disappear. Attempts are already being made in this direction. It is still too early to write with confidence on the measure of success which is to be expected from such endeavors, but the principle is undoubtedly sound. I have had some experience with a preparation known as Secretogen (G. W. Carnrick Co.) and the results have so far seemed to justify the hopes which led to its introduction. It appears to stimulate the gastro-intestinal tract to more vigorous function, and thus to lessen the toxemia. It seems well worth a trial in cases where the poisoning had led to loss of appetite and digestive disturbance.

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Fresh Air Treatment of Tuberculosis.—E. Ward (*The Practitioner,* September, 1918) writing on the curative side of treatment of tuberculosis, says it should be possible to get better results, bearing in mind that in the absence of any specific remedy, the best we can do at present is to raise a patient's resistance to the highest possible level and there maintain it until the disease is arrested and all danger of auto-reinfection has passed (with bacilli present in the sputum this dangerous auto-reinfection period may continue for many years).

Concerning sanatorium treatment he believes that less exposure and more care to prevent chilling patients would widen the scope of these institutions and give better results. Pasteur was able to infect hens with anthrax only after chilling them. At Davos he has been told: "You English doctors treat your sanatorium patients as you would not treat your dogs," meaning that they are too much exposed to all kinds of weather. Possibly it is this common sense application of fresh air, rather than the value of climate, which gives Davos better results than those obtained by sanatoria in healthy places elsewhere.

It has been stated authoritatively, and is therefore generally believed, that cold is the most valuable part of sanatorium treatment, more valuable indeed than the air. "The blood is driven from the skin to the internal organs," it is said, and so forces are concentrated to fight the disease. It is also a matter of tradition in this country, that very little heed need be paid to exposure to cold winds and damp; and patients are said to do better under sanatorium treatment during the winter months. Ward is sure that this is a mistake, and that the future will show how wrong it is. No doubt every sanatorium can show cases which stand the cold successfully, and may even be the better for the exposure; but it is a question of individual constitution and these patients are a minority. It is a case of survival of the fittest. We see the few who have benefited, or at least not suffered, from cold and exposure; the majority who refuse to submit to it, or have failed to stand it, we do not see. Attention to this point might improve considerably our sanatorium results.

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Internal Secretions and Gynecology.—Oliver T. Osborne (*New York Medical Journal,* September 14, 1918) says that total removal of both ovaries is only justifiable in very rare instances. It is unimportant whether it is the ovarian substance or the corpus luteum that furnishes the secretion that is most necessary for the mature woman's mental and physical health; it is a fact that many internal secreting glands are disturbed by the removal of the ovaries. Total removal of the ovarian tissue before puberty stops the development of the genital organs and of the breasts. Total removal after puberty stops menstruation, causes artificial menopause, and multiplies the menopause symptoms and disturbances. The younger the adult woman so castrated, the more serious are the symptoms. Castrated women are often wrecks, both mentally and physically. They may gain weight; they may lose weight; they may be ravenous; they may have no appetite; they may be loquacious; they may be morose; they may be drowsy; they may be sleepless; they may be hysterical; and they may become to all intents and purposes actually insane. Feeding these sufferers ovarian and corpus luteum extracts is only partially successful in ameliorating their condition.

The rules for operation for tubal and ovarian diseases should be:

1. To leave as much of the ovaries as is found healthy.

2. If the operation of necessity destroys the circulation and therefore nutrition of the whole of both ovaries, large grafts from the healthy part of the ovaries should be placed in some location that will allow the ovarian tissue to readily obtain a blood supply and therefore live. If the ovarian transplant lives and functions, it should be remembered that it periodically swells, and hence, intense nondilatable tissue may cause severe pain. The uterine wall, the peritoneum, the labia majora, the mons veneris, the abdominal wall, and even the axilla have all been places suggested for implantation.

3. If there is no healthy ovarian tissue for auto-grafting, and as total extirpation of both diseased ovaries is not an emergency operation, the surgeon connected with a large hospital generally could obtain a piece of healthy ovary from a nonsyphilitic and nontuberculous patient for transplantation into the woman to be castrated. The necessity for obtaining such ovarian tissue would be rare, as total extirpation is rarely needed. Of course the surgeon cannot decide that there is no healthy ovarian tissue until the time of operation, but he should be prepared for such an emergency when there is a probability of the necessity of total extirpation. Ovaries removed from healthy women after sudden accidental death, and properly preserved, would seem to be the ideal tissue.

If these engrafted ovaries or ovarian tissue live and function it may be two or three months before the fact is known by any symptoms or signs in the patient. The signs of success are a general feeling of health, absence or diminution of menopause symptoms, and menstruation. Such grafts may live for a time and then die, but more or less embryonic ovarian tissue may have had time to mature and begin to furnish the secretion so much needed by the patient.

Properly selected patients who have had their ovaries removed for disease and who have psychoses which are not cured by the administration of organic extracts, might be well treated by grafts of healthy human ovarian substance.

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